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Molecular polarisability. The conformations of diacetyl, benzil, and furil as solutes in benzene or carbon tetrachloride. By (Miss) P. H. Cureton, (Mrs.) C. G. Le Fèvre, and R. J. W. Le Fèvre

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510. *The Infrared Spectra of Some Metal Alkoxides, Trialkylsilyloxides, and Related Silanols.*

By C. G. Barraclough, D. C. Bradley, J. Lewis, and I. M. Thomas.

Measurements of the infrared spectra of a number of group IV and group V metal alkoxides, trialkylsilyloxides, and related silanols have been recorded. The silicon–oxygen, carbon–oxygen, and metal–oxygen stretching frequencies have been assigned and the relative magnitude of the frequencies discussed.

The metal trialkylsilyloxides and alkoxides, $M(OSiR_1R_2R_3)_n$ and $M(OR)_n$, are polymeric in some cases.[1,2] The present work has the object of seeking more evidence concerning the nature of the polymers and of determining the characteristic vibrational frequencies of the M–O–Si and M–O–C systems. Data from heats and entropies of vaporisation [3] suggest that the dative bonds from oxygen to metal are relatively weak, with bond strengths of the order of 10 kcal. It may therefore be difficult to confirm the presence of these weak bonds. Additional infrared absorption bands occur in some, but not all, of the polymeric compounds.

Results and Discussion

The infrared spectra of the trialkylsilyloxides and alkoxides, and of related silanols and alcohols were measured in carbon disulphide (Tables 1—5).

1. *The* M–O–Si *System.*—By comparing the spectra of the trialkylsilyloxides and the parent silanols it can be seen that the M–O–Si system has two characteristic frequencies, an intense band about 900 cm.$^{-1}$ and a second, much weaker, band in the 500—600 cm.$^{-1}$

Table 1. *Infrared spectra (cm.$^{-1}$) of metal trialkylsiloxides.*

$Ti[O{\cdot}SiMe_2Pr^i]_4$: 1252vs, 1064w, 998w, 916vs, 880s, 832s, 808s, 776s, 685w, 608vw, 518m
$Zr[O{\cdot}SiMe_2Pr^i]_4$: 1251vs, 999m, 971m, 916vs, 884s, 831s, 808w, 774s, 680w, 594w, 515w
$Ti[O{\cdot}SiMe_2Pr^n]_4$: 1251vs, 1066w, 997w, 917vs, 833s, 804m, 770m, 699w, 521m
$Ta[O{\cdot}SiMe_2Et]_5$: 1250vs, 1156vw, 1066w, 997m, 909vs, 880w, 831m, 806m, 776s, 685s, 595m
$Ta[O{\cdot}SiMeEt_2]_5$: 1250vs, 1240sh, 1010s, 905vs, 797s, 778sh, 755s, 685m, 667sh, 606sh, 592m
$Zr[O{\cdot}SiEt_3]_4$: 1251sh, 1242s, 1017m, 1006m, 966w, 914vs, 941s, 728sh
$Al[O{\cdot}SiEt_3]_3$: 1244s, 1064vs, 1015m, 971w, 810vs, 763w, 741s, 728sh, 638m, 585m, 549w
$Ti[O{\cdot}SiEt_2Me]_4$: 1251s, 1235m, 1016w, 1005w, 915vs, 787s, 756s, 746s, 690w, 673m, 510m
$Zr[O{\cdot}SiEt_2Me]_4$: 1252s, 1236s, 1011m, 1002m, 964m, 912vs, 833m, 799s, 752m, 743m, 683w, 601w, 521m
$Nb[O{\cdot}SiEtMe_2]_5$: 1250vs, 1010m, 957m, 889vs, 839m, 810m, 787s, 752sh, 699m, 617m, 575m
$Ti[O{\cdot}SiMe_3]_4$: 1251vs, 1060w, 1015w, 918vs, 845s, 752s, 685w, 517m, 503w
$Zr[O{\cdot}SiMe_3]_4$: 1251vs, 996w, 971w, 916vs, 839s, 752w, 684w, 521m
$Ti[O{\cdot}SiEtMe_2]_4$: 1251vs, 1241sh, 1058w, 1015w, 960sh, 915vs, 837s, 816s, 784s, 753w, 699m, 629w, 515m
$Zr[O{\cdot}SiEtMe_2]_4$: 1250vs, 1003m, 959m, 913vs, 835s, 781s, 690w
$Hf[O{\cdot}SiEtMe_2]_4$: 1251vs, 1042w, 1014s, 986w, 953sh, 932vs, 837s, 785s, 697m

Abbreviations: vs, very strong; s, strong; m, medium; w, weak; vw, very weak; sh, shoulder; br, broad.

Table 2. *Infrared spectra (cm.$^{-1}$) of metal alkoxides.*

$Ti(OEt)_4$: 1269w, 1136s, 1101s, 1064s, 1042sh, 916s, 885w, 787w, 625–500s
$Ta(OEt)_5$: 1279w, 1163sh, 1149sh, 1117vs, 1072vs, 1030s, 917s, 880s, 556sbr
$Nb(OEt)_5$: 1270w, 1136sh, 1107s, 1063s, 1029sh, 911s, 877w, 835w, 800w, 571sbr
$Ti[O{\cdot}CEt_2Me]_4$: 1294w, 1218w, 1195w, 1163m, 1144s, 1062m, 1939s, 1011s, 993s, 948m, 903m, 883w 811w, 780w, 751w, 737w, 615m, 576w
$Zr[O{\cdot}CEt_2Me]_4$: 1292w, 1220w, 1190w, 1163m, 1150s, 1063s, 1039s, 1010s, 991s, 943s, 903s, 883w, 808w, 775w, 755w 730w, 619w, 559w, 586m, 521m
$Hf[O{\cdot}CMe_3]_4$: 1248sh, 1229sh, 1190s, 1138w, 1015s, 990s, 909sh, 904s, 896sh, 786sh, 781m, 567s, 526m
$Ti[O{\cdot}CHMe_2]_4$: 1163sh, 1126vs, 1005vs, 962sh, 855vs, 826sh, 619vs, 526w
$Zr[O{\cdot}CHMe_2]_4$: 1174vs, 1143vs, 1011vs, 962s, 952w, 943s, 847s, 820s, 559vs, 548s
$Al[O{\cdot}CHMe_2]_3$: 1185s, 1174s, 1138s, 1124s, 1036s, 951s, 861m, 835s, 699m, 678s, 610m, 566s, 535m
$Ta[O{\cdot}CHMe_2]_5$: 1163s, 1130vs, 1001vs, 951sh, 928vw, 848m, 813w, 683w, 540s
$Zr[O{\cdot}CMe_3]_4$: 1235m, 1203s, 1190s, 1065w, 1035sh, 1026sh, 1010sh, 997s, 986sh, 908m, 787w, 781w, 557m, 540m

[1] Bradley and Thomas, *J.*, 1959, 3404.
[2] Bradley, Mehrotra, and Wardlaw, *J.*, 1952, 2027.
[3] Bradley, Mehrotra, Swanwick, and Wardlaw, *J.*, 1953, 2025.

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TABLE 3. *Infrared spectra of trialkylsilanols.*

$Me_3Si{\cdot}OH$: 1252vs, 990s, 966m, 881vs, 842vs, 775sh, 754s, 687w
$EtMe_2Si{\cdot}OH$: 1251vs, 1010s, 960s, 855vs, 837s, 784s, 697m
$Et_2MeSi{\cdot}OH$: 1240s, 1008m, 962m, 847vs, 799s, 766s, 749m, 739sh, 685m, 671w
$Pr^iMe_2Si{\cdot}OH$: 1252vs, 1003m, 976m, 885s, 855vs, 830s, 775s, 680m, 669w
$Et_3Si{\cdot}OH$: 1244s, 1018s, 1007sh, 982s, 966s, 835vs, 813sh, 736s

TABLE 4. *Metal–oxygen and oxygen–silicon stretching frequencies.*

Compound	n *	Si–O	M–O	Compound	n *	Si–O	M–O
$Ti[O{\cdot}SiMe_3]_4$	1·2	918	517	$Zr[O{\cdot}SiEt_2Me]_4$	1·0	912	521
$Ti[O{\cdot}SiEtMe_2]_4$	1·0	915	515	$Zr[O{\cdot}SiEt_3]_4$	1·0	914	—
$Ti[O{\cdot}SiPr^iMe_2]_4$	1·0	916	518	$Hf[O{\cdot}SiEtMe_2]_4$	1·0	932	—
$Ti[O{\cdot}SiPr^nMe_2]_4$	1·0	917	521	$Al[O{\cdot}SiEt_3]_3$	2·0	1,064, 810	638, 585, 549
$Ti[O{\cdot}SiEt_2Me]_4$	1·0	915	510				
$Zr[O{\cdot}SiMe_3]_4$	2·0	916	521	$Nb[O{\cdot}SiEtMe_2]_5$	1·0	889	619, 575
$Zr[O{\cdot}SiEtMe_2]_4$	1·0	913	521	$Ta[O{\cdot}SiEtMe_2]_5$	1·0	909	595
$Zr[O{\cdot}SiPr^iMe_2]_4$	1·0	916	515	$Ta[O{\cdot}SiEt_2Me]_5$	1·0	905	606, 592

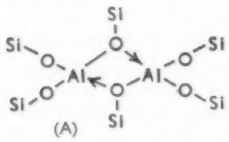
* n = Degree of polymerisation.

TABLE 5. *Infrared spectra of alcohols.*

EtOH: 1081s, 1050s, 876s, 802w
$Me_2CH{\cdot}OH$: 1153s, 1125s, 1070s (C–O stretch), 946s, 813m
$Me_3C{\cdot}OH$: 1234sh, 1205s, 1140s (C–O stretch), 911s, 750m
$Et_2CMe{\cdot}OH$: 1176sh, 1161s, 1133s (C–O stretch), 1055m, 1034sh, 997sh, 973s, 905s, 883sh, 797w, 784w, 772w, 707w

region. The characteristic frequencies for the trialkylsilyloxides are summarised in Table 4. The exceptional data for the aluminium compound will be considered later in this section. It has been suggested[4] that the 900 cm.$^{-1}$ band is an Si–O stretching mode, and in view of its high intensity and the shift in passing to the corresponding silanol, this seems to be correct. We suggest that the band around 500 cm.$^{-1}$ is an M–O stretching mode, by comparison with results for the dichromate ion,[5] where the Cr–O–Cr symmetric and antisymmetric stretches are taken to be 560 cm.$^{-1}$ and 770 cm.$^{-1}$, respectively. Also, in hexamethyldisiloxane the symmetric and antisymmetric stretches in the Si–O–Si skeleton are assigned to 522 cm.$^{-1}$ and 1055 cm.$^{-1}$.[6a] Kriegsmann and Licht[6b] measured both the Raman and infrared spectra of $Ti[O{\cdot}SiMe_3]_4$ and the latter is in good agreement with the present results. Their assignments of the absorption bands at 500 cm.$^{-1}$ and 900 cm.$^{-1}$ agree with ours, although they also tentatively assign several weaker bands to Ti–O and Si–O stretching modes.

The size of the alkyl groups attached to the silicon atom does not affect the frequencies, and even changing the metal has only a small effect on the Si–O stretching frequency. Comparison of quadrivalent and quinquevalent metals suggests that the Si–O stretching vibrations are essentially independent of each other, because in all cases only one band is observed. In the titanium and zirconium compounds only one Si–O stretching vibration should be infrared-active if the M–O–Si groups are linear and the molecule is tetrahedral (the alkyl groups being ignored). However, in the niobium and tantalum compounds with five silyloxy-groups there should be at least two infrared-active Si–O stretching vibrations whatever the geometry of the molecule, if the various Si–O groups interact.



(A)

This is an important point when the spectrum of the aluminium compound is considered because it shows two bands which are both assigned to Si–O stretches on the basis of their high intensity and absence from the parent silanol. This compound is dimeric[7] and can be tentatively formulated as A (alkyl groups being omitted). It is suggested that the 1064 cm.$^{-1}$ band

[4] Zeitler and Brown, *J. Phys. Chem.*, 1957, **61**, 1174.
[5] Stammreich, Bassi, Sala, and Siebert, *Spectrochim. Acta*, 1958, **13**, 192.
[6] (*a*) Kriegsmann, *Z. Elektrochem.*, 1957, **61**, 1088; (*b*) Kriegsmann and Licht, *Z. Elektrochem.*, 1958, **62**, 1163.
[7] Thomas, Ph.D. Thesis, London, 1959.

corresponds to stretching vibrations of the terminal Si–O groups, while the band at 810 cm.$^{-1}$ represents stretching vibrations of the bridging Si–O groups.

The compound $Zr[O{\cdot}SiMe_3]_4$ is also apparently dimeric [1] although it would be expected to be a mixture of monomer and trimer.[8] In either case it should show a second band corresponding to the bridging Si–O group, but no extra band could be found. The O→Zr bond may be appreciably weaker than the O→Al bond and thus lead to a much smaller shift in the Si–O frequency, perhaps only broadening the existing band instead of appearing as a second.

The absence of a band around 520 cm.$^{-1}$ in $Zr[O{\cdot}SiEt_3]_4$ is also difficult to understand, unless it has become much weaker or moved to just below 500 cm.$^{-1}$.

2. *The* M–O–C *System.*—The isopropyl group has [9] characteristic frequencies at 1170, 1150, 950, 920, and 850—750 cm.$^{-1}$. Data for the isopropoxide (Table 2) show the presence of an additional strong band in the 1000 cm.$^{-1}$ region and one or more bands around 550—700 cm.$^{-1}$. In aluminium isopropoxide the isopropyl bands at 1170 cm.$^{-1}$ and 1150 cm.$^{-1}$ are both split into doublets, probably by intramolecular coupling. Our results are in good agreement with those of previous examinations of metal isopropoxides.[4,10] Kreigsmann and Licht [6b] have given assignments for a series of titanium alkoxides, and Guertin *et al.*[11] suggest that bands at 1000 cm.$^{-1}$ in aluminium alkoxides are due to Al–O stretching modes. We consider that these bands are predominantly C–O stretching modes of the Al–O–C groups and that the Al–O stretching modes occur at lower frequencies, not covered by the investigations of Guertin *et al.* A comparison of the metal alkoxides with the corresponding alcohols (Table 5) permits the tentative assignments shown in Table 6. Most of

TABLE 6. *Metal–oxygen and carbon–oxygen stretching frequencies.*

Compound	n *	C–O	M–O
$Ti[O{\cdot}CHMe_2]_4$	1·4	1005	619
$Zr[O{\cdot}CHMe_2]_4$	3·0	1011	559, 548
$Al[O{\cdot}CHMe_2]_3$	3 to 4	1036	699, 678, 610, 566, 535
$Ta[O{\cdot}CHMe_2]_5$	1·0	1001	540
$Zr[O{\cdot}CMe_3]_4$	1·0	997	557, 540
$Hf[O{\cdot}CMe_3]_4$	1·0	990	567, 526
$Ti[O{\cdot}CEt_2{\cdot}Me]_4$	1·0	1011	615, 576
$Zr[O{\cdot}CEt_2{\cdot}Me]_4$	1·0	1010	586, 559, 521
$Ti(OEt)_4$	3·0	1064, 1042	625, 500
$Ta(OEt)_5$	2·0	1072, 1030	556
$Nb(OEt)_5$	2·0	1063, 1029	571

* n = Degree of polymerisation.

the comparisons are obvious but the difficulty in assigning the C–O frequency in alcohols has been discussed by Bellamy,[12] and assignments for the ethoxides must be considered tentative.

The most definite evidence for the assignment of the two C–O stretching modes was obtained from experiments on the hydrolysis of the ethoxides with limited amounts of water.[13] The band at 1030 cm.$^{-1}$ disappears after a relatively small proportion of hydrolysis has taken place but the rest of the spectrum is unaltered. This suggests that the 1030 cm.$^{-1}$ band is associated with bridging ethoxide groups which are removed by hydrolysis, while the 1060 cm.$^{-1}$ band is associated with terminal ethoxide groups which are not hydrolysed until later.

The M–O stretching region of the aluminium isopropoxide spectrum provides more evidence for intermolecular bonding through oxygen atoms. In monomeric aluminium

[8] Bradley, *Nature*, 1958, **182**, 1211.
[9] Sheppard and Simpson, *Quart. Rev.*, 1953, **7**, 19.
[10] Bell, Heisler, Tannenbaum, and Goldenson, *Analyt. Chem.*, 1953, **25**, 1720.
[11] Guertin, Wiberley, Bauer, and Goldenson, *J. Phys. Chem.*, 1956, **60**, 1018.
[12] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen. London, 1958.
[13] Holloway, Ph.D. Thesis, London, 1959.

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isopropoxide there could be a maximum of only three Al–O stretching vibrations, whatever the stereochemistry of the molecule. Actually five bands are observed in this region and the presence of bridging oxygen atoms seems to be the most reasonable explanation. Unfortunately, only one C–O stretching frequency has been definitely identified whereas at least two would be expected. This may arise from the difficulty in assigning frequencies in this part of the spectrum, and the two bands tentatively assigned to coupling of the isopropyl skeletal vibrations may in fact be C–O stretching vibrations.

The monomeric alkoxides show varying numbers of bands in the M–O stretching region but none of them has more bands than would be expected for a monomer, and the variation may be due to steric effects. With the smaller alkyl groups the four oxygen atoms may be arranged tetrahedrally around the central metal atom and there would be only one infrared-active M–O stretching mode. The larger alkyl groups could lead to steric hindrance which would distort the tetrahedron of oxygen atoms and make several of the M–O stretches infrared-active.

With the exception of the ethoxides the C–O stretching frequency falls from the alcohol to the alkoxide. If double bonding occurs between the metal and oxygen, then a contribution from a structure of the type $C-\overset{+}{O}=\overline{M}$ would tend to drain electrons away from the carbon–oxygen σ-bond and weaken it, with a resultant lowering in the C–O stretching frequency. In the case of the trialkylsilyloxides, a rise in the Si–O stretching frequency occurs when the silanolic hydrogen is replaced by a metal although there is still some uncertainty about the positions of the Si–O stretching frequency in the silanols (see Section 3). Comparison of the M–O stretching frequencies in the two series is of interest. For the titanium and zirconium compounds, the M–O frequency rises from trialkylsilyloxide to alkoxide. This can be explained since the silicon atom has available *d* orbitals which compete with the *d* orbitals of the metal in the formation of d_π–p_π bonds with the oxygen atom. The carbon atom in the alkoxide group has no *d* orbital available so that the oxygen atom can only form π-bonds with the metal, thus leading to a higher bond order for the metal–oxygen bond in the alkoxides than for the corresponding bond in the trialkylsilyloxides. The actual degree of this π-bonding may be relatively small in both cases since the M–O frequencies are much lower than the frequencies observed for M=O systems.[14]

3. *The* Si–O–H *System.*—The data for the silanols (Table 3) enable us tentatively to assign the Si–O stretching frequency in these compounds. It has been suggested [15] that this might occur at either 880—830 cm.$^{-1}$ or 1100 cm.$^{-1}$, while Kriegsmann [16] assigns a band at 785 cm.$^{-1}$ in trimethylsilanol as the Si–O stretch. Comparison of Tables 1 and 3 shows that the strong band at 910 cm.$^{-1}$ in the spectra of the trialkylsilyloxides is absent from those of the silanols which show a new strong band in the 880—830 cm.$^{-1}$ region; this new band is assigned to the Si–O stretching vibration in the silanols, and the frequencies are listed in Table 7. The band observed by Kriegsmann at 785 cm.$^{-1}$ is present in both the metal trimethylsilyloxides and trimethylsilanol, whereas the 880 cm.$^{-1}$ band is present only in the latter.

TABLE 7. *Silicon–oxygen stretching frequencies (cm.$^{-1}$) in silanols.*

$Me_3Si{\cdot}OH$, 881; $Me_2SiEt{\cdot}OH$, 855; $Me_2SiPr^i{\cdot}OH$, 855; $Et_2SiMe{\cdot}OH$, 847; $Et_3Si{\cdot}OH$, 835.

The results suggest that there may be some coupling between the Si–O stretching vibration and the rest of the molecular vibrations, since the frequencies fall with increase in size of the alkyl groups. Alternatively, the effect may arise from a variation in the inductive effects of the alkyl groups. The order of magnitude of the Si–O frequency seems correct by comparison of the Si–O–H system, with frequencies of the order of 850

[14] Barraclough, Lewis, and Nyholm, *J.*, 1959, 3552.
[15] Richards and Thompson, *J.*, 1949, 124.
[16] Kriegsmann, *Z. anorg. Chem.*, 1958, **294**, 113.

and 3600 cm.$^{-1}$, with the Si–O–Si group in hexamethyldisiloxane, which has stretching frequencies at 522 and 1055 cm.$^{-1}$.

Experimental

Compounds were prepared as previously described.[1,2,3,7]

Infrared spectra were measured in carbon disulphide by use of a Grubb-Parsons G.S. 2A double-beam grating spectrometer. The trialkylsilyloxides and alkoxides were measured as 25% (wt./vol.) solutions in a 0·03-mm. potassium bromide cell. The polymeric compounds were also examined as 1% (wt./vol.) solutions in a 1-mm. cell, but in all cases the spectra were identical with the results obtained in the more concentrated solutions. The silanols and alcohols were examined as 1% (wt./vol.) solutions in a 1-mm. potassium bromide cell. Spectra were recorded over the range 500—1300 cm.$^{-1}$.

William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1.
Department of Chemistry,
University of Western Ontario, London, Ontario. [*Received, November 16th*, 1960.]

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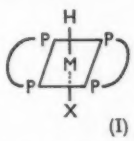
511. *Hydrido-complexes of Ruthenium*(II) *and Osmium*(II).

By J. Chatt and R. G. Hayter.

A series of hydrido-complexes of the types *trans*-[MHX(chelate)$_2$] (I) (M = Ru, Os; X = Cl, Br, I, H, SCN, CN, NO_2; chelate = a chelating ditertiary phosphine) has been prepared and shown to have considerable thermal stability, especially when the diphosphine contains aromatic groups. The unique hydrogen atom shows a large chemical shift in the nuclear magnetic resonance spectrum and causes an absorption band (ν_{M-H}) (M = Ru, Os) in the infrared spectrum in the region 1600—2050 cm.$^{-1}$. The dipole moments (X ≠ H) are of the order 5 D. The effect of X on ν_{M-H} is discussed and a possible correlation with kinetic data suggested.

After the discovery of planar hydrido-complexes of platinum(II) [1] stabilised by tertiary phosphines, and possibly of the unstable analogous compounds of palladium(II) [1] and nickel(II),[2] we set out to prepare similar octahedral complexes and here we describe the preparation and properties of ruthenium and osmium hydrido-complexes of the general types *trans*-[MHX(diphosphine)$_2$] (I).[3]



(I)

M = Ru, Os.
X = Cl, Br, I, H, SCN, CN, or NO_2.
P–P = $C_2H_4(PR_2)_2$ (R = Me, Et, Ph), $CH_2(PPh_2)_2$, or o-$C_6H_4(PEt_2)_2$.

The ruthenium and osmium compounds are similar in properties, those of osmium being slightly more stable thermally but more rapidly oxidised by air.

Hydrido-Complexes of Ruthenium(II).—The complex hydrido-halides of ruthenium(II), which are all of *trans*-configuration, were prepared by reduction of the dihalogeno-complexes,[4] *cis*-[RuX_2(diphosphine)$_2$] (X = Cl, Br, or I), with lithium aluminium hydride in ether or tetrahydrofuran, followed by treatment with ethanol to destroy any residual

[1] Chatt, Duncanson, and Shaw, *Proc. Chem. Soc.*, 1957, 343.
[2] Green, Street, and Wilkinson, *Z. Naturforsch.*, 1959, **14b**, 738.
[3] For preliminary communications see: Chatt and Hayter, *Proc. Chem. Soc.*, 1959, 153; Chatt, Hart, and Hayter, *Nature*, 1960, **187**, 55.
[4] Chatt and Hayter, *J.*, 1961, 896.

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tetrahydride, dihydride, or AlH_4^- complexes which had been produced. The *trans*-dihalides were not reduced by this reagent.

The hydrido-halides are colourless or pale yellow crystalline solids, often melting without decomposition in a vacuum, and thermally stable to about 300°. The solid hydrides decompose slowly in contact with moist air, the rate of decomposition decreasing roughly in order of ligands:

$$o\text{-}C_6H_4(AsMe_2)_2 > C_2H_4(PMe_2)_2 > C_2H_4(PEt_2)_2 > o\text{-}C_6H_4(PEt_2)_2 \approx CH_2(PPh_2)_2$$

The complex $[RuHCl\{o\text{-}C_6H_4(AsMe_2)_2\}_2]$ was too unstable to be crystallised or fully characterised; *trans*-$[RuHCl\{CH_2(PPh_2)_2\}_2]$ darkens slowly in air over a period of days. The hydrides are soluble in most organic solvents, those with the aliphatic ligands being very soluble even in light petroleum. The complex *trans*-$[RuHCl\{C_2H_4(PMe_2)_2\}_2]$ is also soluble in dilute aqueous ammonia and was recovered in good yield on rapid neutralisation with dilute hydrochloric acid. An excess of acid gave hydrogen and *cis*-$[RuCl_2\{C_2H_4(PMe_2)_2\}_2]$. Treatment of *trans*-$[RuHCl\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ with an equivalent of hydrogen chloride in ether gave a mixture of *trans*- (25%) and *cis*-dichloro-complex (75%).

The chloride ion in *trans*-$[RuHCl\{C_2H_4(PR_2)_2\}_2]$ (R = Me, Et) is labile, as it is in *trans*-$[PtHCl(PR_3)_2]$,[5] and it can be replaced by iodide, thiocyanate, cyanide, or nitrite anions, on treatment with the corresponding alkali-metal salt, as well as by hydrogen on treatment with lithium aluminium hydride. This lability contrasts with the inertness of the chloride ion in *trans*-$[RuCl_2\{C_2H_4(PR_2)_2\}_2]$. The chloride ion in

trans-$[RuHCl\{CH_2(PPh_2)_2\}_2]$

is inert, probably owing to steric hindrance by the phenyl groups.

trans-$[RuHCl\{C_2H_4(PEt_2)_2\}_2]$

was recovered unchanged after attempts at alkylation with diazomethane or with ethylene at 80°/40 atm. The hydrido-complexes obtained are listed in Table 1, together with certain physical properties. It was not possible to obtain *trans*-$[RuHCl\{C_2H_4(PPh_2)_2\}_2]$ because the corresponding *cis*-dichloro-complex [4] is not available for reduction.

The two complex ruthenium dihydrides in Table 2 were prepared by reduction of the corresponding hydrido-halide, *trans*-[RuHX(diphosphine)$_2$], or *cis*-dihalide with lithium aluminium hydride, the use of hydroxylic solvents being avoided. They are paler, more soluble and more rapidly oxidised by air than the corresponding hydrido-halides.

Hydrido-complexes of Osmium(II).—The complex hydrido-halides and dihydrides of osmium were prepared similarly to those of ruthenium (see Table 1). Since

cis-$[OsCl_2\{C_2H_4(PPh_2)_2\}_2]$

is available *trans*-$[OsHCl\{C_2H_4(PPh_2)_2\}_2]$,$C_6H_6$ was obtained, although the corresponding ruthenium compound is unknown.

The chloro-complexes of ruthenium(II) with the ligands $[CH_2]_n(PPh_2)_2$ ($n = 1$ or 2) tend to solvate; this tendency is more marked with osmium. Thus,

trans-$[OsCl_2\{[CH_2]_n(PPh_2)_2\}_2]$

crystallises as a solvate with chloroform, which is retained in a vacuum at 80°, while *trans*-$[OsHCl\{[CH_2]_n(PPh_2)_2\}_2]$ crystallises with a tightly-held molecule of benzene. In the hydrido-chloride ($n = 1$), the benzene is not removed by crystallisation from ethyl acetate and has the unusual property of suppressing the band due to the Os–H stretching vibration in the infrared spectrum. This benzene is about 50% removed by evacuation at 100° for 48 hr. and the infrared spectrum (Nujol mull) then shows a weak ν_{Os-H} band at 2077 cm.$^{-1}$. If this compound is prepared in the absence of benzene, it crystallises solvated from ethyl acetate and its infrared spectrum then shows strong bands due to ν_{Os-H} (2074 cm.$^{-1}$) and $\nu_{C=O}$ (1735 cm.$^{-1}$). Models show that the benzene molecule is a suitable size to fit in the cavity above the hydridic hydrogen. This is unlikely to suppress the Os–H stretching vibration completely, but probably makes it inactive in the infrared region.

[5] Basolo, Chatt, Gray, Pearson, and Shaw, *J.*, 1961, 2207.

The complex *trans*-[RuHCl{$CH_2(PPh_2)_2$}$_2$] was similarly solvated with $\frac{1}{2}C_6H_6$ or 1·5EtOAc, but the solvent was not so tightly held and ν_{Ru-H} was still observed.

Structure.—The *trans*-octahedral structure of the hydrido-chlorides and dihydrides of ruthenium and osmium was established by dipole moment and nuclear magnetic resonance

TABLE 1. *Tertiary phosphine and arsine hydrido-complexes of ruthenium*(II) *and osmium*(II).

	Compound	M. p. (vacuum)	Colour *	Dipole moment (D)	ν_{Ru-H} (cm.$^{-1}$) ‡	Chemical shift (p.p.m., H_2O standard)
I	*trans*-[RuHCl{$C_2H_4(PEt_2)_2$}$_2$]	174·5—176°		4·9 [c]	1938	+27·1 [c]
II	*trans*-[RuHBr{$C_2H_4(PEt_2)_2$}$_2$]	188—190 †	Yellow	5·65 [c]	1945	+26·3 [c]
III	*trans*-[RuHI{$C_2H_4(PEt_2)_2$}$_2$]	212—224 †	Yellow	5·8	1948	+24·6 [c]
IV	*trans*-[RuH(SCN){$C_2H_4(PEt_2)_2$}$_2$]	245—249 †		—	1919	—
V	*trans*-[RuH(CN){$C_2H_4(PEt_2)_2$}$_2$] [a]	—		—	1803	—
VI	*trans*-[RuH_2{$C_2H_4(PEt_2)_2$}$_2$]	147—153		2·1 [c]	1615 [f]	—
VII	*trans*-[RuHCl{$C_2H_4(PMe_2)_2$}$_2$]	217—221		4·8 [c]	1891	—
VIII	*trans*-[RuHBr{$C_2H_4(PMe_2)_2$}$_2$]	215—220 † [d]	Yellow	—	1895	—
IX	*trans*-[RuHI{$C_2H_4(PMe_2)_2$}$_2$]	322 †	Yellow	—	1898	—
X	*trans*-[RuH(SCN){$C_2H_4(PMe_2)_2$}$_2$]	240 †		—	1870 [b]	—
XI	*trans*-[RuH(CN){$C_2H_4(PMe_2)_2$}$_2$]	230 †	Yellow	—	1754 [b]	—
XII	*trans*-[RuH(NO_2){$C_2H_4(PMe_2)_2$}$_2$]	240 †	Yellow	—	1858 [b]	—
XIII	*trans*-[RuHCl{*o*-$C_6H_4(PEt_2)_2$}$_2$]	250—256 †	Yellow	4·45 [c]	1978 [b] (br)	—
XIV	*trans*-[RuHI{*o*-$C_6H_4(PEt_2)_2$}$_2$]	278—283 †	Brown	—	1976 [b] (br)	—
XV	*trans*-[RuH_2{*o*-$C_6H_4(PEt_2)_2$}$_2$]	276·5—278·5 †	Yellow	1·2 [c]	1617 [b]	—
XVI	*trans*-[RuHCl{$CH_2(PPh_2)_2$}$_2$],$\frac{1}{2}C_6H_6$	283—284·5 †	Yellow	4·95 [c]	1978 [f]	—
XVII	*trans*-[RuHCl{*o*-$C_6H_4(AsMe_2)_2$}$_2$] [a]	190 † [d]		—	1804	—
XVIII	*trans*-[OsHCl{$C_2H_4(PEt_2)_2$}$_2$]	170·5—171·5		4·6 [c]	2039	+31·3
XIX	*trans*-[OsHI{$C_2H_4(PEt_2)_2$}$_2$]	224—231	Yellow	—	2051	+26·1
XX	*trans*-[OsH(SCN){$C_2H_4(PEt_2)_2$}$_2$]	200 †		—	2009	
XXI	*trans*-[OsH_2{$C_2H_4(PEt_2)_2$}$_2$]	150—155		—	1721 [f]	—
XXII	*trans*-[OsHCl{$C_2H_4(PMe_2)_2$}$_2$]	190—205 †		5·05 [c]	2014 [f]	—
XXIII	*trans*-[OsHCl{$C_2H_4(PPh_2)_2$}$_2$],C_6H_6	313·5—318 †	Yellow	—	2046 [f]	—
XXIV	*trans*-[OsHCl{$CH_2(PPh_2)_2$}$_2$],C_6H_6	294·5—298·5 †	Yellow	3·85	2045 [b]	—
XXV	*trans*-[OsH_2{*o*-$C_6H_4(PEt_2)_2$}$_2$]	293—297	Lemon	—	1720 [b]	—

* Colourless unless stated. † With decomp. ‡ n-Hexane solutions unless marked.
[a] Not pure. [b] Benzene solution. [c] Chloroform solution. [d] In air. [e] Calc. from estimated values of densities and refractivities. [f] Nujol mull.

measurements. The moments of the hydrido-chlorides are in the range 3·8—5·0 D, similar to that of *trans*-[$PtHCl(PEt_3)_2$] (4·2 D).

The chemical shifts of the unique protons in the complex hydrides (see Table 1) are large, even for transition-metal hydrides. The proton resonance consists of five equally spaced bands with intensities roughly in the ratios 1 : 4 : 6 : 4 : 1, although, in some cases, only the three more intense centre bands were visible. This pattern confirms the *trans*-configuration, being consistent with the coupling of the hydrogen nucleus to four equivalent phosphorus nuclei, each of spin $\frac{1}{2}$.

If these large chemical shifts were due entirely to diamagnetic shielding, the hydridic hydrogen would appear to be associated with about twice as many electrons as the hydrogen in water, whose chemical shift relative to the unshielded proton is +27 p.p.m. The hydridic hydrogen should thus be negatively charged but the dipole moments indicate that it carries a slight positive charge; evidently diamagnetic shielding is not the main cause of the large shifts, and it seems likely that some other effect, such as paramagnetic circulation on the metal atom, is mainly responsible.[6]

Infrared Spectra.—The infrared spectra of the complex hydrido-halides show strong metal–hydrogen stretching bands (ν_{M-H}) in the region 1800—2050 cm.$^{-1}$ (see Table). This assignment was confirmed from the infrared spectrum (hexachlorobutadiene mull) of

[6] Bishop, Down, Emtage, Richards, and Wilkinson, *J.*, 1959, 2484.

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trans-[RuDCl{$C_2H_4(PEt_2)_2$}$_2$] (prepared from *cis*-[$RuCl_2${$C_2H_4(PEt_2)_2$}$_2$] and $LiAlD_4$) which showed a weakened ν_{Ru-H} band at 1954 cm.$^{-1}$, as well as a new partially obscured band at 1410 cm.$^{-1}$ (ν_{Ru-D}) [isotopic shift factor $(1{\cdot}92)^{-1}$]. Another new band was observed in the spectrum of the deuteride at 516 cm.$^{-1}$, and was tentatively assigned to δ_{R-D}. The corresponding region in the spectrum of the hydride was obscured by strong absorption. ν_{M-H} is about 100 cm.$^{-1}$ higher in an osmium compound than in the corresponding ruthenium compound.

The frequencies, ν_{M-H}, in the compounds *trans*-[$MHX\{C_2H_4(PR_2)_2\}_2$] (M = Ru, Os; R = Me, Et) are of interest because they depend markedly on the anionic ligand X and can be correlated with certain kinetic data, as they can in the analogous series of platinous complexes *trans*-[$PtHX(PEt_3)_2$]. In the platinum series the sequence of decreasing ν_{Pt-H} is $X = NO_3 > Cl > Br > I > NO_2 > SCN > CN$.[7] This is closely similar to the sequence of decreasing reactivity of the group X in [Pt dien X]$^+$ in reaction with pyridine where the order is $NO_3 > Cl > Br > I > SCN > NO_2 > CN$ [8] and to the *trans*-effect series as established by Russian workers.[9,7]

Such extensive data are not available in the ruthenium and osmium series of complexes but signs of a similar relationship can be found. The sequence of ν_{M-H} (M = Ru, Os) in complexes of $C_2H_4(PR_2)_2$ (R = Me, Et) (see Table 1) is $I > Br > Cl > SCN > NO_2 > CN > H$. The complexes of the *o*-phenylenediphosphine give broad bands whose positions are not as well defined. This sequence shows a gross similarity to that of the platinous compounds, *viz.*, halide > (SCN, NO_2) > CN, but is different in detail, notably in the reversed sequence of the halides. Kinetic data on the displacement of X from ruthenium(II) and osmium(II) complexes are not available, but in the displacement of X by water from the cobalt(III) complexes $[Co(NH_3)_5X]^+$, which are isoelectronic in the valency shell, the order of decreasing reactivity of X is $I > Br > Cl > SCN > NO_2$,[10] in which the reversed order of halogens also appears. No *trans*-effect series has been established for ruthenium(II) or osmium(II) complexes, but we know qualitatively that the hydride ion has a high *trans*-effect (p. 2606), as in the platinous series,[5] and so should occur near CN in the *trans*-effect series. It is observed near CN in the ν_{Ru-H} series, and if the value of ν_{Ru-H} is a reliable guide it has an even greater *trans*-effect than CN, hitherto considered to have the greatest *trans*-effect of anionic ligands.

Thus it appears that a similar relationship between ν_{M-H}, lability, and *trans*-effect of the anionic ligands, X, may exist in both octahedral and square-planar complexes. There are slight differences in the detailed sequence of the ligands X when they are arranged in order of the magnitudes of the above effects, depending mainly on the metal in the complex. These differences are probably related to differences in the π-bonding capacities of the metals, as suggested by Basolo, Gray, and Pearson [8] in discussing the kinetic series. The " platinum sequence " would be characteristic of the stronger dative π-bonding metals and the " ruthenium–osmium sequence " of moderately dative π-bonding metals. The same distinction may also apply to square-planar *versus* octahedral complexes in general, because in square-planar complexes with the vacant p_z-orbital, dative π-bonding is enhanced by *dp*-hybridisation.[11]

The chelating ligand also influences ν_{M-H} in the hydrido-halide complexes. Thus in the series *trans*-[RuHCl(chelate)$_2$] ν_{M-H} falls from 1978 to 1804 cm.$^{-1}$ in a sequence which appears to be roughly that of decreasing electronegativity and double-bonding capacity of the ligands, *viz.*, *o*-$C_6H_4(PEt_2)_2 \approx CH_2(PPh_2)_2 > C_2H_4(PEt_2)_2 > C_2H_4(PMe_2)_2 >$ *o*-$C_6H_4(AsMe_2)_2$.

[7] Chatt, Duncanson, and Shaw, *Chem. and Ind.*, 1958, 859.
[8] Basolo, Gray, and Pearson, *J. Amer. Chem. Soc.*, 1960, **82**, 4200.
[9] See Hel'man, *Izvest. Sekt. Platiny drug. blagorod. Metal., Inst. obshchei neorg. Khim.*, 1954, **28**, 88.
[10] See Basolo and Pearson, " Mechanisms of Inorganic Reactions," John Wiley and Sons, Inc., New York, 1958, p. 122.
[11] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.

Experimental

Microanalyses were by the Microanalytical Department of these Laboratories. M. p.s were determined on a Kofler hot stage, unless otherwise stated. The complex hydrides were manipulated in an atmosphere of dry nitrogen. Light petroleum was the fraction of b. p. 60—80°. For the dihalogeno-complexes used in the following preparations see ref. 4.

Preparation of Hydrido-complexes of Ruthenium(II) *and Osmium*(II).—(i) *Hydrido-halides.* *cis*-Dichlorodi-{1,2-bis(diethylphosphino)ethane}ruthenium (0·20 g.) was dissolved in dry tetrahydrofuran (10 ml.) and treated with an excess of lithium aluminium hydride in tetrahydrofuran under nitrogen. The original yellow solution rapidly became colourless and, after 5 minutes' refluxing, ethanol was slowly added until effervescence ceased. Solvent was then removed at 12 mm. and the benzene-soluble portion of the white residue crystallised from light petroleum, yielding pure trans-*hydridochlorodi*-{1,2-*bis*(*diethylphosphino*)*ethane*}*ruthenium*(II) (I) (0·13 g., 61%) as needles, decomp. 310° in a vacuum (Found: C, 43·6; H, 9·0; Cl, 2·1%; *M*, ebullioscopically in benzene, 570. $C_{20}H_{49}ClP_4Ru$ requires C, 43·7; H, 9·0; Cl, 6·45% *M*, 550). This compound has a magnetic susceptibility in the solid state of $-0{\cdot}45 \times 10^{-6}$ c.g.s. units.

The following compounds were similarly prepared from the corresponding *cis*-dihalogeno-complexes:

trans-*Hydridobromodi*-{1,2-*bis*(*diethylphosphino*)*ethane*}*ruthenium*(II) (II) (50% yield), tablets from light petroleum (Found: C, 39·9; H, 8·3. $C_{20}H_{49}BrP_4Ru$ requires C, 40·4; H, 8·3%).

trans-*Hydridoiododi*-{1,2-*bis*(*diethylphosphino*)*ethane*}*ruthenium*(II) (III) (55% yield), feathery plates from light petroleum (Found: C, 37·5; H, 7·7%; *M*, ebullioscopically in benzene, 622. $C_{20}H_{49}IP_4Ru$ requires C, 37·45; H, 7·7%; *M*, 641·5), magnetic susceptibility $-1{\cdot}0 \times 10^{-6}$ c.g.s. units in the solid state.

trans-*Hydridochlorodi*-{1,2-*bis*(*dimethylphosphino*)*ethane*}*ruthenium*(II) (VII) (35% yield), needles from light petroleum (Found: C, 33·1; H, 7·3. $C_{12}H_{33}ClP_4Ru$ requires C, 32·9; H, 7·6%), sublimes unchanged in a vacuum at 120° and decomposes at ~300°.

trans-*Hydridobromodi*-{1,2-*bis*(*dimethylphosphino*)*ethane*}*ruthenium*(II) (VIII) (32%), needles from light petroleum (Found: C, 29·7; H, 6·9. $C_{12}H_{33}BrP_4Ru$ requires C, 29·9; H, 6·9%), sublimes at <280°.

trans-*Hydridoiododi*-{1,2-*bis*(*dimethylphosphino*)*ethane*}*ruthenium*(II) (IX) (55%), needles (Found: C, 27·3; H, 6·2; I, 24·3. $C_{12}H_{33}IP_4Ru$ requires C, 27·2; H, 6·3; I, 24·0%).

trans-*Hydridochlorodi*-{o-*phenylenebis*(*diethylphosphine*)}*ruthenium*(II) (XIII) (75%), prisms from 2 : 1 benzene–light petroleum (Found: C, 51·8; H, 7·6%; *M*, ebullioscopically in 1·2% benzene solution, 674; in 1·57% solution, 650. $C_{28}H_{49}ClP_4Ru$ requires C, 52·05; H, 7·6%; *M*, 646).

trans-*Hydridoiododi*-{o-*phenylenebis*(*diethylphosphine*)}*ruthenium*(II) (XIV) (70%), from 2 : 1 benzene–light petroleum (Found: C, 45·5; H, 6·7. $C_{28}H_{49}IP_4Ru$ requires C, 45·6; H, 6·7%).

trans-*Hydridochlorodi*-{1,2-*bis*(*diphenylphosphino*)*methane*}*ruthenium*(II) (XVI) (75%), prisms from 2 : 1 benzene–light petroleum, crystallising with 0·5 mol. of benzene, which is not removed in a vacuum at 100° in 48 hr. (Found: C, 67·5; H, 5·4. $C_{53}H_{48}ClP_4Ru$ requires C, 67·3; H, 5·1%). Subsequent crystallisation from ethyl acetate yielded yellow needles, m. p. 287·5—289° (decomp.; in a vacuum) (Found: C, 64·8; H, 5·4. $C_{50}H_{45}ClP_4Ru,1{\cdot}5CH_3{\cdot}CO_2C_2H_5$ requires C, 64·8; H, 5·5%). The infrared spectrum (Nujol mull) showed a strong band at 1735 cm.$^{-1}$ due to $\nu_{C=O}$ of the ester.

trans-*Hydridochlorodi*-{1,2-*bis*(*diethylphosphino*)*ethane*}*osmium*(II) (XVIII) (47%), needles (from light petroleum), decomp. *ca.* 315° in a vacuum (Found: C, 37·95; H, 7·7. $C_{20}H_{49}ClOsP_4$ requires C, 37·6; H, 7·7%).

trans-*Hydridoiododi*-{1,2-*bis*(*diethylphosphino*)*ethane*}*osmium*(II) (XIX) (45%), needles from light petroleum (Found: C, 32·8; H, 6·8. $C_{20}H_{49}IOsP_4$ requires C, 32·9; H, 6·8%). This compound was also prepared from the hydrido-chloride by treatment with lithium iodide in acetone and was identified by its infrared spectrum.

trans-*Hydridochlorodi*-{1,2-*bis*(*dimethylphosphino*)*ethane*}*osmium*(II) (XXII) (21%), sublimed in a vacuum at 180° (Found: C, 27·1; H, 6·3. $C_{12}H_{33}ClOsP_4$ requires C, 27·35; H, 6·3%).

trans-*Hydridochlorodi*-{1,2-*bis*(*diphenylphosphino*)*ethane*}*osmium*(II) (XXIII) (40%), plates

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(from 5 : 1 benzene–light petroleum), solvated with a molecule of benzene (Found: C, 63·1; H, 5·2. $C_{58}H_{55}ClOsP_4$ requires C, 63·2; H, 5·0%).

trans-*Hydridochlorodi*-{1,2-*bis*(*diphenylphosphino*)*methane*}*osmium*(II) (XXIV) (85%), needles (from 1 : 1 benzene–light petroleum), solvated with a molecule of benzene [Found: C, 62·3; H, 4·9%; *M*, ebullioscopic in benzene, 1157 (0·24% solution), 1108 (0·65%). $C_{56}H_{51}ClOsP_4$ requires C, 62·6; H, 4·8%; *M*, 1074]. Recrystallisation from ethyl acetate gave lemon-yellow needles, m. p. 294—296° (decomp.; in a vacuum), unchanged in infrared spectrum and analysis (Found: C, 62·3; H, 4·9%). Approximately half the solvated benzene was removed *in vacuo* at 100° in 48 hr. (Found: C, 61·2; H, 5·0. $C_{53}H_{48}ClOsP_4$ requires C, 61·55; H, 4·7%).

This compound was also prepared in the absence of benzene, ethyl acetate being used as solvent for crystallisation, and was obtained as yellow needles, m. p. 291—294° (decomp.; in a vacuum) (Found: C, 60·3; H, 4·8. $C_{50}H_{45}ClOsP_4$ requires C, 60·3; H, 4·6. $C_{50}H_{45}ClOsP_4,\frac{1}{2}CH_3{\cdot}CO_2C_2H_5$ requires C, 60·1; H, 4·75%). The infrared spectrum (Nujol mull) shows the presence of ν_{Os-H} (2074 cm.$^{-1}$), as well as bands due to ethyl acetate at 1735, 1235, and 1048 cm.$^{-1}$.

(ii) *Metathetical replacement reactions.* (*a*) *trans*-Hydridochlorodi-{1,2-bis(diethylphosphino)ethane}ruthenium(II) (0·10 g.) was dissolved in acetone (5 ml.) and treated with a solution of potassium thiocyanate (0·20 gm.) in acetone (5 ml.) under nitrogen. An immediate white precipitate appeared and, after 5 minutes' warming on a steam-bath, the solution was filtered and the solvent removed at 12 mm. The benzene-soluble portion of the white solid residue was crystallised from light petroleum, yielding pure trans-*hydridothiocyanatodi*-{1,2-*bis*-(*diethylphosphino*)*ethane*}*ruthenium*(II) (IV) as needles (0·03 g., 31%) (Found: C, 43·5; H, 8·35; N, 2·5. $C_{21}H_{49}NP_4RuS$ requires C, 44·0; H, 8·6; N, 2·45%), $\nu_{max.}$ (in hexane) 2090s cm.$^{-1}$ (C≡N).

Similarly prepared were the following:

trans-*Hydridothiocyanatodi*-{1,2-*bis*(*dimethylphosphino*)*ethane*}*ruthenium*(II) (X), prisms (from 1 : 1 benzene–light petroleum) (50%) (Found: C, 33·7; H, 7·45. $C_{13}H_{33}NP_4RuS$ requires C, 33·9; H, 7·2%), $\nu_{max.}$ (in Nujol) 2098s cm.$^{-1}$ (C≡N).

trans-*Hydridothiocyanatodi*-{1,2-*bis*(*diethylphosphino*)*ethane*}*osmium*(II) (XX), needles (22%) (from light petroleum) (Found: C, 38·4; H, 7·5; N, 2·3. $C_{21}H_{49}NOSP_4$ requires C, 38·1; H, 7·5; N, 2·1%), $\nu_{max.}$ (in hexane) 2101 cm.$^{-1}$.

(*b*) trans-*Hydridocyanodi*-{1,2-*bis*(*dimethylphosphino*)*ethane*}*ruthenium*(II) (XI) was obtained when *trans*-[RuHCl{$C_2H_4(PMe_2)_2$}$_2$] (0·15 g.) in acetone (10 ml.) was refluxed with potassium cyanide (0·2 g.) in water (3 ml.) under nitrogen for 15 min.; the acetone layer then decanted and evaporated and the benzene-soluble residue crystallised from 1 : 1 benzene–light petroleum (20% yield; needles) (Found: C, 35·2; H, 7·8; N, 2·8. $C_{13}H_{33}NP_4Ru$ requires C, 36·45; H, 7·8; N, 3·3%); $\nu_{max.}$ (Nujol mull) 2062vs cm.$^{-1}$.

A similar attempt to prepare *trans*-[RuH(CN){$C_2H_4(PEt_2)_2$}$_2$] (V) in dry acetone was only partially successful, the infrared spectrum (Nujol mull) of the product showing bands due to unchanged hydrido-chloride (1948 cm.$^{-1}$) and to hydrido-cyanide (2069 and 1807 cm.$^{-1}$).

Similarly prepared was trans-*hydridonitrodi*-{1,2-*bis*(*dimethylphosphino*)*ethane*}*ruthenium*(II) (XII) needles (50%) (from 3 : 7 benzene–light petroleum) (Found: C, 32·2; H, 7·3; N, 3·4. $C_{12}H_{33}NO_2P_4Ru$ requires C, 32·1; H, 7·4; N, 3·1%), $\nu_{max.}$ (Nujol mull) 1300s, 1258s, and 803s cm.$^{-1}$ (NO_2).

(iii) *Dihydrides.* *trans*-Hydridochlorodi-{1,2-bis(diethylphosphino)ethane}ruthenium(II) (0·20 g.) in dry tetrahydrofuran (10 ml.) was treated with an excess of lithium aluminium hydride in tetrahydrofuran. The pale yellow solution immediately became colourless. After 5 min., the solution was filtered and evaporated in a stream of nitrogen, leaving a mixture of colourless solid and oil. The solid was extracted into light petroleum and crystallisation afforded pure trans-*dihydridodi*-{1,2-*bis*(*diethylphosphino*)*ethane*}*ruthenium*(II) (VI) as prisms (52 mg., 27%). This distils at about 160° and decomposes at 280° in an evacuated tube (Found: C, 46·4; H, 9·7. $C_{20}H_{50}P_4Ru$ requires C, 46·6; H, 9·8%).

trans-Dihydridodi-{1,2-bis(diethylphosphino)ethane}osmium(II) (XXI) was similarly prepared in 50% yield (prisms from light petroleum). A good analysis was not obtained, further crystallisation or distillation resulting in a slightly poorer analysis (Found: C, 40·9; H, 8·5. Calc. for $C_{20}H_{50}OsP_4$: C, 39·7; H, 8·3%). The infrared spectrum (Nujol mull) of the product is identical with that of *trans*-[RuH_2{$C_2H_4(PEt_2)_2$}$_2$], apart from the metal–hydrogen stretching bands.

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Analogously prepared from the corresponding *cis*-dichloro-complexes were trans-*dihydridodi*-{o-*phenylenebis*(*diethylphosphine*)}-*ruthenium*(II) (XV), prisms (50%) (from benzene) (Found: C, 54·9; H, 8·2. $C_{28}H_{50}P_4Ru$ requires C, 55·0; H, 8·2%), and -*osmium*(II) (XXV), prisms (70%) (from benzene) (Found: C, 48·2; H, 7·25. $C_{28}H_{50}OsP_4$ requires C, 48·0; H, 7·2%).

Physical Measurements.—The dipole moments were determined as described in ref. 12 and are recorded in Table 2. The moments of all the dihydrido-complexes were low, indicating a *trans*-configuration, but because of their great sensitivity to air and moisture exact moments were not determined.

TABLE 2. *Dipole moments.*

Compound	$10^3\omega$	$\Delta\varepsilon/\omega$	$10^2\Delta n/\omega$	$-\Delta v/\omega$	$_TP$	$_EP$	$_OP$	Dipole moment (D)
I	3·293	5·242						
	7·038	5·260						
	5·269			0·323				
	7·824			0·358	676	(165)	487 *	4·9 *
II	7·208	6·145		(0·37)	826 *	(149)	655 *	5·65 *
III	3·401	6·150						
	6·270	6·152						
	19·32		7·90					
	28·96		8·71					
	4·281			0·297				
	5·400			0·370	889	173	691	5·8
VII	3·523	6·228						
	5·026	6·145		(0·35)	614 *	(124)	471 *	4·8 *
XVI	1·406	3·284		(0·35)	804 *	(261)	504 *	4·95 *
XIII	5·483	3·709						
	5·692	3·689		(0·35)	604 *	(176)	401 *	4·45 *
XVIII	1·764	3·743						
	2·724	3·766		(0·35)	604 *	(145)	437 *	4·6 *
XII	1·496	5·294						
	3·209	5·253		(0·35)	649 *	(108)	524 *	5·05 *
XXIV	1·804	2·157						
	2·977	2·109						
	21·80		14·39					
	27·48		14·56					
	4·043			0·519	632	285	304	3·85

Estimated values are in parentheses. * Calc. from estimated values of densities and refractivities.

The magnetic resonance of the hydrogen nucleii was obtained at 40 Mc with a Varian Associates 4300B spectrometer, flux stabilisation and sample spinning being used. The chemical shifts were measured against cyclohexane as an internal standard on a scale defined so that the value for cyclohexane itself is +3·9. This scale for non-polar sôlvents approximates to one based on water as zero in aqueous solution. Addition of 4·66 to each chemical shift converts it to the τ scale.

The infrared spectra were recorded on a Grubb–Parsons G.S.2A spectrometer.

The authors are indebted to Dr. D. M. Adams for measurement and discussion of the infrared spectra and Dr. N. Sheppard for measuring the nuclear magnetic resonance spectra.

IMPERIAL CHEMICAL INDUSTRIES LIMITED,
AKERS RESEARCH LABORATORIES,
THE FRYTHE, WELWYN, HERTS, ENGLAND. [*Received, November 17th,* 1960.]

[12] Chatt and Shaw, *J.*, 1959, 705.

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512. *Molecular Polarisability. The Anisotropies of the Molecules* PCl_3, $OPCl_3$, NMe_3, *and* $ONMe_3$.

By N. Hacket and R. J. W. Le Fèvre.

The increase of molecular refractivity from trimethylamine to the oxide and the decrease from phosphorus trichloride to oxychloride have been investigated by determining the principal polarisabilities of these molecules. The polarisability of trimethylamine becomes greater, both along and across the direction of action of the resultant molecular dipole moment, when the oxide is formed. With phosphorus trichloride, addition of an oxygen atom notably reduces the polarisability across $\mu_{resultant}$. Attempts to calculate principal polarisabilities by using empirical equations involving bond lengths, stretching frequencies, etc., are reasonably satisfactory in three cases, but for phosphorus oxychloride, b_1 emerges *ca.* 20% too large, although a contraction in $b_2 = b_3$ from phosphorus trichloride is qualitatively predicted.

Molar Kerr constants at infinite dilution, ${}_\infty({}_mK_2)$, are here recorded at 25° for phosphorus trichloride and oxychloride in benzene and for trimethylamine oxide in dioxan. From the observed dipole moments, molecular refractions, etc., and with an assumption that these molecules have rotational symmetry about the direction of action of $\mu_{resultant}$, estimates of the principal polarisabilities follow, as in Table 1.

Table 1. *Molar Kerr constants, moments, and principal polarisabilities.*

Solute	Solvent	$10^{12}\,{}_\infty({}_mK_2)$	μ, D *	$10^{23}(b_1 + 2b_2)$	$10^{23}b_1$	$10^{23}(b_2 = b_3)$
PCl_3	Benzene	$-10{\cdot}9_2$	$0{\cdot}89_0$	3·012	0·914	1·049
$OPCl_3$	,,	$-73{\cdot}8_4$	$2{\cdot}42_5$	2·936	0·902	1·017
$ONMe_3$	Dioxan	210·0	5·03	2·505	0·885	0·810

* Calc. by taking the distortion polarisation as $1{\cdot}05R_D$.

Discussion.—None of these three compounds has previously been examined in this way, nor does the literature indicate the degrees of anisotropy to be expected for the bonds between phosphorus and chlorine or oxygen, or between nitrogen and oxygen. It has, however, been noted [1] with phosphorus trichloride and oxychloride that the smaller molecule has the larger molecular refraction, *i.e.* that the addition of an oxygen atom to the trichloride *reduces* the average polarisability. The results in Table 1 suggest that the diminution occurs more in b_2 than in b_1. Unfortunately, owing to the smallness of $\mu_{resultant}$ for phosphorus trichloride, its precise value is much affected by the distortion polarisation, ${}_DP$, used in its extraction from the ${}_\infty P_2$ observed. A moment of 0·89 D is given when ${}_DP = 1{\cdot}05R_D = 27{\cdot}6$ c.c. Grassi,[2] from a study of the total polarisation of phosphorus trichloride as a vapour, records the temperature-invariant term in the Debye equation $P = A + B/T$ as 32·2 c.c.; taking 32·2 c.c. as ${}_DP$ yields $\mu_{PCl_3} = 0{\cdot}75_3$ D, and in consequence $10^{23}b_1 = 0{\cdot}858$ and $10^{23}\,(b_2 = b_3) = 1{\cdot}077$. Nevertheless, although b_1 for $OPCl_3$ now appears larger than that for PCl_3, we see that diminution of b_2 from PCl_3 to $OPCl_3$ is still the preponderant change, and evidently that which makes R_{PCl_3} greater than R_{OPCl_3}.

The cases of trimethylamine and its oxide differ from those of the phosphorus halides. Aroney and Le Fèvre [3] found for trimethylamine $10^{23}b_1 = 0{\cdot}774$ and $10^{23}(b_2 = b_3) = 0{\cdot}763$; addition of oxygen therefore increases *both* b_1 and b_2, the former ($\Delta b_1 = 0{\cdot}111$) more than the latter ($\Delta b_2 = 0{\cdot}047$), consistently with R_{ONMe_3} exceeding R_{NMe_3}.

The causes of these changes in polarisability seem unlikely to be entirely structural in origin because the Y–X bonds in the YX_3 portions of the two oxygenated molecules are,

[1] Ingold, " Structure and Mechanism in Organic Chemistry," Cornell University Press, New York, 1953.
[2] Grassi, *Nuovo Cimento*, 1933, **10**, 3.
[3] Aroney and Le Fèvre, *J.*, 1958 3002.

if anything, slightly more splayed than when in the free YX_3 molecules, a circumstance which—provided $b_L^{P\text{-}Cl} > b_T^{P\text{-}Cl} = b_V^{P\text{-}Cl}$—should tend to make b_2 for $OPCl_3$ larger than b_2 for PCl_3. More probably the process of attaching an oxygen atom in fact changes the polarisabilities of the C–N and Cl–P links in opposite ways. We note that from NMe_3 to $ONMe_3$ the intercentre distance [4] r_{N-O} *increases* by 0·12 Å, while from PCl_3 to $OPCl_3$ r_{P-Cl} diminishes from 2·04 to 1·99 Å. These facts can be reconciled by the arguments of Walsh [5] according to which bond length and bond polarity vary together. The establishment of the strongly [6] polar NO and PO bonds will, by induction, augment the component moments of the C→N bonds and reduce those of the Cl←P bonds; the alterations of r_{XY} from YX_3 to OYX_3 are therefore understandable.

Longitudinal bond polarisabilities and bond lengths. Two [7] empirical connections (equations A and B) between these properties have been suggested:

$$10^{24} b_L^{X\text{-}Y} = 0{\cdot}140 + 0{\cdot}156 d^3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (A)$$

where d is the intercentre distance r_{XY}, or if Y is a terminal atom, the sum of r_{XY} and the radius of Y, r_Y (*i.e.* 0·995 for chlorine), and

$$\nu_{XY} = 9273Q - 254 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (B)$$

where $Q = (b_L^{X\text{-}Y}/M)^{\frac{1}{2}}/r^2_{XY}$; ν_{XY} being the stretching frequency of the bond X–Y in cm.$^{-1}$, and M is the reduced mass of X–Y.

In the present instances, data taken as in Table 2 lead to the values of b_L^{XY} shown. The

TABLE 2. *Calculation of longitudinal polarisabilities by equations A and B.*

Molecule	XY	r_{XY} (Å)	ν_{XY} (cm.$^{-1}$)	$10^{23} b_L$ (from eqn. A)	$10^{23} b_L$ (from eqn. B)
PCl_3	P–Cl	2·043	488	$0{\cdot}45_1$	$0{\cdot}61_6$
$OPCl_3$	P–Cl	1·99	485	$0{\cdot}42_9$	$0{\cdot}52_6$
,,	PO	1·45	1290	?	$0{\cdot}45_3$
NMe_3	C–N	1·47	?	0·050	?
$ONMe_3$	C–N	1·59	?	0·063	?
,,	NO	1·36	960	?	$0{\cdot}10_6$

values of r_{XY} are as listed in ref. 4. The two P–Cl frequencies are given by Daasch and Smith,[8] that for PO is from Gore [9] and papers cited by him, while ν_{NO} is midway between the limits 950—970 cm.$^{-1}$ reported by Mathis, Wolf, and Gallais.[10] Owing to the absence of definite information regarding r_{YO} for " true " single and " true " double bonds between Y and oxygen (cf. equation iii in ref. 7*a*), and because ν_{O-N} is uncertain in aliphatic amines generally (cf. Bellamy, ref. 11), Table 2 cannot be completed; nevertheless the opposite trends in b_L^{XY} from YX_3 to OYX_3 are correctly predicted.

Transverse bond polarisabilities. Vogel [12] has recorded dispersion measurements of refractivity from which R_∞ for PCl_3 and $OPCl_3$ may be deduced as 25·33 and 24·69 c.c., respectively; from the former the total polarisability ($b_L^{P\text{-}Cl} + 2b_T^{P\text{-}Cl}$) of the P–Cl link is $1{\cdot}004 \times 10^{-23}$ c.c. (strictly this total must include contributions due to the lone-pair electrons of the phosphorus atom; an analogous remark applies, of course, to Aroney and Le Fèvre's discussion [3] of the N–H and N–C bonds). The apparent transverse polarisability of P–Cl in PCl_3 is therefore $0{\cdot}194 \times 10^{-23}$ c.c. Since there is no clear way of disentangling

[4] " Tables of Interatomic Distances and Configuration in Molecules and Ions," Chem. Soc. Spec. Publication No. 11, 1958.
[5] Walsh, *Trans. Faraday Soc.*, 1946, **42**, 56; 1947, **43**, 60; *Ann. Reports*, 1947, **44**, 32.
[6] Smyth, " Dielectric Behaviour and Structure," McGraw-Hill, New York, Toronto, London, 1955 p. 245.
[7] Le Févre, *Proc. Chem. Soc.*, (*a*) 1958, 283; (*b*) 1959, 363.
[8] Daasch and Smith, *Analyt. Chem.*, 1951, **23**, 853.
[9] Gore, *Discuss. Faraday Soc.*, 1950, **9**, 138.
[10] Mathis, Wolf, and Gallais, *Compt. rend.*, 1956, **242**, 1873.
[11] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 221.
[12] Vogel, *J.*, 1948, 1833.

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the refractivities of the P–Cl and the PO links in phosphorus oxychloride, we assume that the ratio b_L^{P-Cl}/b_T^{P-Cl} is the same in phosphorus trichloride and oxychloride; accordingly b_L^{P-Cl} in $OPCl_3$ appears as $0{\cdot}164 \times 10^{-23}$. If $(b_L + 2b_T)$ for C–N is the same in trimethylamine as in the oxide, the values of b_L^{C-N} in Table 2 correspond to values of b_T^{C-N} of $0{\cdot}07_2$ and $0{\cdot}06_6 \times 10^{-23}$, respectively. (In this paragraph, for want of guiding information, we presume the two transverse polarisabilities of the P–Cl, PO, and NO bonds to be equal, *e.g.*, $b_T^{P-Cl} = b_V^{P-Cl}$.)

Predictions of molecular polarisabilities. With the geometrical details appropriate for these molecules, their principal polarisabilities may be estimated. The Cl·P·Cl angles are [4] 100·1° in phosphorus trichloride and 103·6° in the oxychloride. By symmetry the resultant dipole moment μ_{res} in each structure will act along the rotational axis, parallel to which also one of the principal molecular polarisabilities, b_1, is measured; b_2 and b_3, the two other polarisabilities, relate to directions which are mutually perpendicular, and also perpendicular to that of b_1. The angles between μ_{res} and a P–Cl bond follow as 62° 16′ in phosphorus trichloride and 65° 10′ in the oxychloride. Introduction of the appropriate polarisabilities for PCl and PO therefore yields:

$$10^{23}b_1^{PCl_3} = 0{\cdot}856 \text{ and } 10^{23}b_1^{OPCl_3} = 1{\cdot}133.$$

From R_∞, we know $(b_1 + 2b_2)$, so that

$$10^{23}b_2^{PCl_3} = 1{\cdot}078 \text{ and } 10^{23}b_2^{OPCl_3} = 0{\cdot}901_5.$$

In trimethylamine oxide the C·N·C angle is reported by Lister and Sutton [13] as 109·5°, *i.e.*, within the limits (108° ± 4°) given in ref. 4 for trimethylamine itself; $(b_1 + 2b_2)$ for trimethylamine is $2{\cdot}299_5$ and for trimethylamine oxide is $2{\cdot}505 \times 10^{-23}$. Calculated values follow as in Table 3.

TABLE 3. *Predicted and found principal molecular polarisabilities.*

	$10^{23}b_1$ calc.	$10^{23}(b_2 = b_3)$ calc.	$10^{23}b_1$ found	10^{23} $(b_2 = b_3)$ found
PCl_3	0·856	1·078	0·914 (0·858) *	1·049 (1·077) *
$OPCl_3$	1·133	0·902	0·902	1·017
NMe_3	0·785	0·757	0·774 †	0·763 †
$ONMe_3$	0·879	0·813	0·885	0·810

* Bracketed values are obtained if μ is taken as $0{\cdot}75_3$ D; see discussion above.
† From ref. 3.

The only seriously incorrect prediction is that for phosphorus oxychloride. Perhaps the empirical equations are inapplicable to bonds—such as PO—involving *d*-orbitals; alternatively, 1290 cm.$^{-1}$ may not be the appropriate frequency in this case. To obtain $b_1^{OPCl_3} = 0{\cdot}902 \times 10^{-23}$ requires ν_{PO} to be 964 cm.$^{-1}$.

EXPERIMENTAL

Materials, Methods, etc.—The two phosphorus halides were B.D.H. products, redistilled as required, fractions with b. p. 75—76° (trichloride) and 106—107° (oxychloride) at 760 mm. being taken. Trimethylamine oxide hydrate, prepared according to Meisenheimer,[14] was dehydrated by sublimation at 150°/5 mm., and stored *in vacuo* over phosphorus pentoxide; it had m. p. 220°. Benzene and dioxan were purified by refluxing them over, and then distilling them from, sodium–potassium alloy or sodium, respectively, immediately before making up solutions. Obvious precautions against moist air were taken in all transference operations; unless the dioxan solutions were kept thoroughly dry the insoluble hydrate of trimethylamine oxide was gradually precipitated and prevented electric birefringence measurements.

Apparatus, techniques, symbols used, and methods of calculation, have been as described before.[15,16] Observations are recorded in Table 4 and results summarised in Table 5. The

[13] Lister and Sutton, *Trans. Faraday Soc.*, 1939, **35**, 495.
[14] Meisenheimer, *Annalen*, 1913, **397**, 286.
[15] Le Fèvre and Le Fèvre, *J.*, 1953, 4041; 1954, 1577; *Rev. Pure Appl. Chem.*, 1955, **5**, 261.
[16] Le Fèvre, "Dipole Moments," Methuen, London, 3rd Edn., 1953, Chap. 2.

quantities $\Delta\varepsilon$, Δd, Δn, and ΔB are the differences found between the dielectric constants, densities, refractive indexes, and Kerr effects, respectively, of the solvents and of solutions containing weight fractions w_2 of solute. The following data apply at 25° to the two solvents involved:

	ε_1	d_1	$(n_1)_D$	p_1 (c.c.)	C	H	J	$B_1 \times 10^7$	${}_eK_1 \times 10^{12}$
Dioxan...	2·2090	1·0280	1·4202	0·27942	0·16473	2·008	0·4752	0·068	0·01162
Benzene	2·2725	0·87378	1·4973	0·34086	0·18809	2·114	0·4681	0·410	0·0756

TABLE 4. *Dielectric-constant, density, etc., increments from solvent to solutions.*

Phosphorus trichloride in benzene

10^5w_2	1530	3823	6055	6708	7757	9278	9568	10,602	10,665	11,912	14,452	16,788	20,141
$10^4\Delta\varepsilon$	—	—	—	469	545	685	—	—	761	847	1039	1175	1434
$10^5\Delta d$	611	1509	2380	—	—	—	3831	4278	—	—	—	—	—
10^5w_2	4082	5747	8567	11,634	12,045	16,033	21,039	26,770	27,802	29,725	31,808	32,264	
$10^{10}\Delta B$	−22	−27	−43	−56	−62	−82	−102	−137	−143	−161	−168	−171	

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 0{\cdot}712$; $\Sigma\Delta d/\Sigma w_2 = 0{\cdot}399$; $\Sigma\Delta b/\Sigma w_2 = -0{\cdot}516 \times 10^{-7}$.

Phosphorus oxychloride in benzene

10^5w_2	2272	3393	4497	6951	9223	12,700		
$10^4\Delta\varepsilon$	955	1425	1949	2977	4012	5670		
$10^5\Delta d$	954	1439	1912	2994	4020	5639		
10^5w_2	1369	1433	1541	2637	3936	4359	5447	5483
$10^{10}\Delta B$.....	−28	−30	−31	−58	−85	−94	−120	−122

whence $\Delta\varepsilon = 4{\cdot}13w_2 + 0{\cdot}219w_2^2$; $\Delta d = 0{\cdot}415w_2 + 0{\cdot}0195w_2^2$; $10^7\Delta B = -2{\cdot}041w_2 - 3{\cdot}12w_2^2$.

Trimethylamine oxide in dioxan

10^5w_2	122	181	237	307	392	446	494	532
$10^4\Delta\varepsilon$	521	781	975	1303	1654	1884	2073	2173
$10^5\Delta d$	−10	−11	−16	−22	−25	−29	−31	−37
10^5w_2	101	104	133	141	142	170	185	201	242
$10^{10}\Delta B$.....	19	19	23	26	24	30	35	31	45
10^5w_2	249	264	269	330	337	345	371	395	
$10^{10}\Delta B$.....	45	47	48	57	59	61	65	67	
10^5w_2	237	392	494					
$10^5\Delta n$	10	19	29					

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 41{\cdot}9$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}0668$; $\Sigma\Delta B/\Sigma w_2 = 17{\cdot}64$; $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}0516$.

TABLE 5. *Calculation of results.*

Solute	Solvent	$\alpha\varepsilon_1$	β	γ	δ	$\infty\,({}_mK_2) \times 10^{12}$
PCl_3	Benzene	$0{\cdot}71_2$	0·399	0·003	$-1{\cdot}25_{85}$	$-10{\cdot}9_2$
$OPCl_3$	,,	4·13	0·475	−0·015	$-4{\cdot}97_8$	$-73{\cdot}8_4$
$ONMe_3$	Dioxan	41·9	−0·065	0·036	259·5	210·0

	∞P_2 (c.c.)	${}_DP$ (c.c.)	μ (D)	$(\theta_1 + \theta_2) \times 10^{35}$	${}_RP$ (c.c.)
PCl_3	43 8	27·6 [a]	$0{\cdot}89_0$	$-2\ 59_6$	25·33 [b]
,,	,,	32·2 [c]	$0{\cdot}75_3$	,,	,,
$OPCl_3$	146·6	26·3 [a]	$2{\cdot}42_5$	$-17{\cdot}5_6$	24·69 [b]
$ONMe_3$	540·8	22·7 [a]	5·03	$49{\cdot}9_4$	21·07 [d]

a, *i.e.* 1·05 R_D; *b* extrapolated from *R*'s given by Vogel [12]; *c* from Grassi [2]; *d* *i.e.* 0·97R_D.

Previous Determinations of Dipole Moments.—Wesson [17] lists values, obtained in benzene or carbon tetrachloride, from 0·70 to 0·90 D for phosphorus trichloride, and between 2·36 and 2·42 D for the oxychloride; the trichloride is stated to show $\mu = 1{\cdot}89$ D in dioxan. Change of solvent does not affect trimethylamine oxide so markedly, Linton [18] reporting 5·02 D in dioxan, against Phillips, Hunter, and Sutton's moment of 4·87 D in benzene.[19]

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, November 28th*, 1960.]

[17] Wesson, " Tables of Electric Dipole Moments," Technology Press, M.I.T., 1948.
[18] Linton, *J. Amer. Chem. Soc.*, 1940, **62**, 1945.
[19] Phillips, Hunter, and Sutton, *J.*, 1945, 146.

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513. *Molecular Rearrangements. Part VI.* The Thermal Rearrangement of* N-*Methyl*-N-p-*nitrophenylnitramine.*

By T. J. Barnes and W. J. Hickinbottom.

N-Methyl-*N*-*p*-nitrophenylnitramine, when heated at its melting point or in an indifferent solvent, rearranges to *N*-methyl-2,4-dinitroaniline; also formed are nitric oxide, formaldehyde, *N*-methyl-*p*-nitroaniline, and 2,4-dinitroaniline.

The rearrangement is prevented if the nitramine is heated with 2,6-dimethyl- or 2,6-di-isopropyl-phenol; good yields of *N*-methyl-*p*-nitroaniline and of the appropriate 2,6-dialkyl-*p*-nitrophenols are obtained. With 2,6-di-t-butylphenol, the formation of the nitrophenol is accompanied by the production of nitric oxide, 3,3′,5,5′-tetra-t-butyl-4,4′-diphenoquinone, and some 4,4′-dihydroxy-3,3′,5,5′-tetra-t-butylbiphenyl.

It is evident that the nitro-group of the nitramine can be transferred in good yield to the nucleus of a suitable phenol. Evidence on the course of this nitration has been obtained from the behaviour of the nitramine in *NN*-diethylaniline and in alkylbenzenes.

The significance of these observations is discussed in relation to the course of the rearrangement.

In contrast to the volume of work on the acid-catalysed rearrangement of arylnitramines to nitroanilines,[1] the only recorded observation on the thermal rearrangement is by Bamberger and Landsteiner.[2] They found that heating phenylnitramine gave mainly *o*-nitroaniline with some *p*-nitroaniline, *o*- and *p*-nitrophenol, nitrosobenzene, carbon dioxide, nitrogen, and nitrous fumes. The present work is a further study of the thermal isomerisation of arylnitramines. For this purpose *N*-methyl-*N*-*p*-nitrophenylnitramine seemed suitable: it can give only one normal product of rearrangement; the *N*-methyl group prevents the complication of prototropic change to the *aci*-nitro-form; and a nitro-group seemed preferable for blocking the *para*-position since halogen may be expelled as halogen hydride [3] and an alkyl group may be oxidised.

Decomposition of *N*-methyl-*N*-*p*-nitrophenylnitramine at its melting point is rapid and not easily controlled; the main reaction—formation of *N*-methyl-2,4-dinitroaniline—is accompanied by formation of nitric oxide, formaldehyde, *N*-methyl-*p*-nitroaniline, and a small amount of a nitrosamine. In an indifferent solvent, such as tetrachloroethane, the change proceeds more smoothly with the formation of the same products, together with 2,4-dinitroaniline.

It is evident that the thermal rearrangement is accompanied by oxidation of the *N*-methyl group to formaldehyde and expulsion of the nitro-group as nitric oxide. It was, therefore, of interest to observe how the nitramine behaved in solvents sensitive to oxidation or to nitration, *e.g.*, phenols. It is known [4] that arylnitramines are converted into the corresponding amine with loss of the *N*-nitro-group when heated with phenol, although sulphuric acid is generally added to assist the reaction. Nothing is known of the fate of the phenol in these reactions or yet of the displaced nitro-group.

When phenol and *N*-methyl-*p*-nitrophenylnitramine are heated together, denitration of the nitramine to give *N*-methyl-*p*-nitroaniline was approximately quantitative. Identification of the products from the phenol presented unexpected difficulties. More satisfactory

* Part V, Elkobaisi and Hickinbottom, *J.*, 1960, 1286.

[1] Cf. Hughes and Ingold, *Quart. Rev.*, 1952, **6**, 34.
[2] Bamberger and Landsteiner, *Ber.*, 1893, **26**, 488.
[3] Orton and Smith, *J.*, 1902, **81**, 806; 1905, **87**, 389; 1907, **91**, 146.
[4] Mertens, *Ber.*, 1886, **19**, 2126; Van Romburgh, *Rec. Trav. chim.*, 1886, **5**, 241; 1887, **6**, 370; 1880, **7**, 230; Pinnow, *Ber.*, 1897, **30**, 837, 838; Reverdin, *Bull. Soc. chim. France*, 1911, **9**, 43; 1912, **11**, 485; 1915, **17**, 190; *Ber.*, 1914, **47**, 1537; Reilly and Hickinbottom, *J.*, 1919, **115**, 175; Clarkson, Holden, and Malkin, *J.*, 1950, 1556; Sommer, *J. prakt. Chem.*, 1903, **67**, 534; Hollingsworth, *J.*, 1959, 2424.

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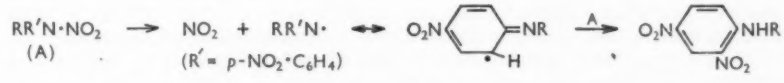
results were obtained by using 2,6-dialkylphenols; these are only feebly acidic and cannot act to a major extent as proton-catalysts for the rearrangement; they are also sufficiently sensitive to oxidation to be used as indicators for any oxidising action. In 2,6-di-t-butylphenol, 4-nitro-2,6-di-t-butylphenol was formed in about 70% yield; other products were nitric oxide, 3,3′,5,5′-tetra-t-butyl-4,4′-diphenoquinone, and the corresponding dihydroxybiphenyl. In 2,6-di-isopropylphenol, the yield of the 4-nitrophenol was about 70%; in 2,6-dimethylphenol the yield of nitration product was about 90% and no 3,3′,5,5′-tetramethyl-4,4′-diphenoquinone was detected in the products. 4-Nitro-2,6-di-t-butylphenol is known [5] to decompose when heated to give nitric oxide and 3,3′,5,5′-tetra-t-butyl-4,4′-diphenoquinone; when 2,6-di-t-butylphenol is heated with the nitramine, part, at least, of the diphenoquinone is formed by thermal decomposition of the nitrophenol, and this view is confirmed by the fact that by using lower temperatures or other 2,6-dialkylphenols, the yield of nitrophenol may be increased to about 90% at the expense of the diphenoquinone.

That the *N*-nitro-group of the nitramine can be transferred intact to another kind of molecule under suitable conditions is important in considering the course of the rearrangement of arylnitramines to nitroanilines. It strongly suggests that the migration of the nitro-group, brought about thermally, is not intramolecular but involves a rupture of the $N–NO_2$ bond in such a way that the nitro-group is free to nitrate if conditions are suitable.

It is possible to infer, with some certainty, the nature of this bond fission from observations on the thermal decomposition of the nitramine in diethylaniline. There is no recognisable attack on the aromatic nucleus which is sensitive to electrophilic reagents; the *N*-nitro-group is thus not available as an electrophilic nitrating agent. Instead the *N*-ethyl group is oxidised to acetaldehyde, by, it may be assumed, a free-radical attack; [6] similar oxidation of the *N*-methyl group of *N*-methyl-*p*-nitrophenylnitramine occurs during thermal rearrangement of this nitramine.

A free-radical mechanism for the thermal rearrangement and decomposition of the arylnitramine is supported by the behaviour of *N*-methyl-*p*-nitrophenylnitramine in boiling solution in the alkylbenzenes. The only reactions are oxidation of the side chain of the aromatic hydrocarbon with concurrent replacement of the *N*-nitro-group of the *N*-nitramine by hydrogen; rearrangement of the nitramine to the corresponding *N*-methyl-2,4-dinitroaniline also occurs. Oxidation of the side chain of the alkylbenzene is in accord with all previous observations on the behaviour of alkylbenzenes towards free-radical oxidation and halogenation; it excludes the possibility that the *N*-nitro-group reacts as an electrophilic reagent.

It it is accepted that rearrangement and decomposition of the nitramine are by a free-radical mechanism, the thermal rearrangement can be represented by the annexed scheme. Here nitric oxide and formaldehyde are also formed as minor products and it seems a reasonable assumption that the nitric oxide is derived from nitrogen dioxide as



a result of oxidation of the *N*-methyl group to formaldehyde, which is supported by the observations of Glazer *et al.*[7] on the dealkylation of tertiary amines by oxides of nitrogen. An alternative explanation that oxidation of the *N*-methyl group arises from reduction of the *N*-nitramine to an *N*-nitrosamine is, however, not yet excluded by the experimental evidence.

[5] Barnes and Hickinbottom, *J.*, 1961, 953.
[6] Henbest and Thomas, *J.*, 1957, 3032.
[7] Glazer, Hughes, Ingold, James, Jones, and Roberts, *J.*, 1950, 2668.

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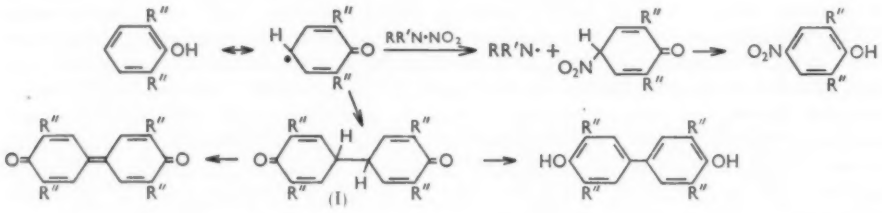
Nitration of 2,6-dialkylphenols by *N*-methyl-*p*-nitrophenylnitramine can be explained on the scheme propounded for the thermal decomposition of the nitramine. Substantial support for the first stage of the further reactions shown is provided by the isolation of



the dihydroxybiphenyl from the products of this nitration. It is already known [5] that compound (I) isomerises readily to the corresponding phenol, and that it can be oxidised to the corresponding diphenoquinone.

Experimental

N-Methyl-*N*-*p*-nitrophenylnitramine, prepared by Hughes and Jones's method,[9] freed from acid by repeated treatment with dilute aqueous ammonia, and crystallised from ethanol, had m. p. 141° (decomp.).

For thermal decomposition of the nitramine, a round-bottomed flask was used, heated by an oil-bath and attached through a condenser to two cold traps, the first cooled in solid carbon dioxide and ethanol, the second by liquid nitrogen. A slow stream of nitrogen was passed through the apparatus during the experiment.

The identity of the products was confirmed whenever practicable by mixed m. p. determination and comparison of the infrared spectrum with that of an authentic specimen.

Thermal Decomposition of N-*Methyl*-N-p-*nitrophenylnitramine.*—(a) *Solid.* The nitramine (20 g.) in contact with the walls of the flask began to darken at 138° (bath-temperature); at 139—140° it melted, with swelling and bubbling. It was often impossible to prevent an evolution of gas so rapid that the connections with the cold trap were forced apart with the development of olive-brown fumes; there was also a smell of formaldehyde and of nitroaniline.

When the decomposition was complete, there remained a dark brown tar, and similar material had been projected into the condenser and carried over into the first cold trap.

The gaseous products were nitric oxide (condensed as a blue solid in the second cold trap) and formaldehyde (dimedone derivative and colour reactions).

From the solid products, *N*-methyl-*p*-nitroaniline (m. p. 150—151°; *N*-nitroso-derivative, m. p. 100—100·5°) was extracted from their benzene solution with hydrochloric acid. The non-basic products, after evaporation of the benzene, were extracted with light petroleum (b. p. 60—80°) to remove a small amount of a nitrosamine, m. p. 91—92·5°, probably *N*-methyl-*N*-*p*-nitrophenylnitrosamine (the amount did not permit identification). The remainder, consisting of *N*-methyl-2,4-dinitroaniline, was purified to m. p. 174—175° by a preliminary crystallisation from aqueous acetic acid, dissolution in benzene to remove more tar, treatment of the benzene solution with charcoal, and filtration through alumina. The ratio of *N*-methyl-*p*-nitroaniline to *N*-methyl-2,4-dinitroaniline was ~1 : 8.

(b) *In* 1,1,2,2-*tetrachloroethane.* A solution of the nitramine (15 g.) in purified tetrachloroethane (150 c.c.) began to darken at about 95° and evolution of gas was first evident at 103°. As the temperature was raised, the solution rapidly became red. In the meantime the evolution of gas continued at the b. p. of the solvent and showed signs of slackening only after 8 hr.; it was substantially complete after 10 hr.

The products were nitric oxide, water, formaldehyde, *N*-methyl-*p*-nitroaniline (2 g., 18%),

[8] Kharasch and Joshi, *J. Org. Chem.*, 1957, **22**, 1439.
[9] Hughes and Jones, *J.*, 1950, 2678.

N-methyl-2,4-dinitroaniline (9·6 g., 64%), and tar (2·1 g.). In the more soluble fractions of the recrystallisation of methyldinitroaniline, the presence of 2,4-dinitroaniline was recognised by diazotisation and coupling with β-naphthol to give the azo-β-naphthol, m. p. and mixed m. p. 302°.

In another experiment the yields were: formaldehyde, as dimedone derivative 4%; *N*-methyl-*p*-nitroaniline, 23%; *N*-methyl-2,4-dinitroaniline, 59%.

(c) *In phenols.* (i) When the nitramine (1·97 g.) and 2,6-di-t-butylphenol (7·2 g.) were heated together, slow evolution of gas began at about 140° and the colour of the melt, initially yellow, darkened as the temperature was raised and as the gas evolution increased. After 2 hr., when the temperature was 200°, there was no perceptible gas evolution.

The only gaseous product was nitric oxide; formaldehyde was not detected.

The phenolic melt was steam-distilled to remove unchanged 2,6-di-t-butylphenol, m. p. 37° (5·05 g.) (Found: C, 81·6; H, 10·6. Calc. for $C_{14}H_{22}O$: C, 81·5; H, 10·7%), and the remainder, dissolved in ether, was extracted with hydrochloric acid to remove *N*-methyl-*p*-nitroaniline (m. p. 152—152·5°; 1·45 g., 95%; nitrosamine, m. p. 100—101°). The non-basic products were separated by treatment with aqueous alkali into 3,5,3′,5′-tetra-t-butyl-4,4′-diphenoquinone, m. p. 247—248° (0·40 g.) (Found: C, 82·5; H, 9·7. Calc. for $C_{28}H_{40}O_2$: C, 82·3; H, 9·9%), and 4-nitro-2,6-di-t-butylphenol, m. p. 156·5° (1·85 g., 73%) (Found: C, 66·7; H, 8·2; N, 5·4%; *M*, 247. Calc. for $C_{14}H_{21}O_3N$: C, 66·9; H, 8·4; N, 5·6%; *M*, 251) [α-naphthylurethane, m. p. 199·5—200° (Found: C, 71·6; H, 6·5; N, 6·6. Calc. for $C_{25}H_{28}N_2O_4$: C, 71·4; H, 6·7; N, 6·7%)]. From the more soluble fractions in the purification of the diphenoquinone 0·15 g. of 4,4′-dihydroxy-3,5,3′,5′-tetra-t-butylbiphenyl was isolated as pale yellow needles, m. p. 184°, readily converted into the diphenoquinone even when boiled in alcohol with charcoal.

(ii) The nitramine (1·97 g.) and 2,6-di-isopropylphenol (6·24 g.) were heated together at 110—114° for 90 min. The products were nitric oxide (small yield), 2,6-di-isopropyl-4-nitrophenol, m. p. 112° (1·51 g., 68%) (Found: C, 64·7; H, 7·6; N, 6·5. Calc. for $C_{12}H_{17}NO_3$: C, 64·6; H, 7·7; N, 6·3%), 3,3′,5,5′-tetraisopropyl-4,4′-diphenoquinone (Found: C, 81·7; H, 9·0. Calc. for $C_{24}H_{32}O_2$: C, 81·8; H, 9·15%), m. p. 214° (0·3 g.), *N*-methyl-*p*-nitroaniline (1·25 g., 82%), and *N*-methyl-*N*-*p*-nitrophenylnitrosamine (0·25 g., 14%). In the isolation of these products, it was more convenient, after the excess of di-isopropylphenol had been removed by steam-distillation, to extract the nitrophencl first with alkali. The remainder of the product was then extracted (Soxhlet) by water; the diphenoquinone remained insoluble. The mixture of methylnitroaniline and nitrosamine was separated by chromatography on a silica–Celite 535 column with benzene–light petroleum (b. p. 40—60°).

(iii) The nitramine (1·97 g.) and 2,6-dimethylphenol (4·28 g.), heated together at 115—128° for 3 hr., gave 2,6-dimethyl-4-nitrophenol, m. p. 172—173° (1·45 g., 87%), and a mixture of *N*-methyl-*p*-nitroaniline with some of its nitrosamine. 3,3′,5,5′-Tetramethyl-4,4′-diphenoquinone was not detected.

(d) *In alkylbenzenes* (in part with C. Beard). (i) The nitramine (50 g.) and *p*-xylene (100 g.) were boiled together for 3 days during which there was evolution of nitrous fumes. The xylene solution was extracted with aqueous sodium carbonate to remove *p*-toluic acid and then steam-distilled. The residue consisted of *N*-methyl-*p*-nitroaniline, m. p. 150—151°, and *N*-methyl-2,4-dinitroaniline, m. p. 177·5—178·5°. The steam-distillate consisted of *p*-xylene with *p*-tolualdehyde (1·5 g.) (2,4-dinitrophenylhydrazone, m. p. 240—241°; phenylhydrazone, m. p. 112°).

(ii) When the nitramine (15 g.) and mesitylene (50 c.c.) were boiled together for 5 hr., the products were nitric oxide, formaldehyde (0·03 g.), 3,5-dimethylbenzoic acid (0·1 g.), *N*-methyl-*p*-nitroaniline (9·3 g.), *N*-methyl-2,4-dinitroaniline (1·1 g.), and tar (0·9 g.).

(iii) Cumene (50 c.c.) and *N*-methyl-*N*-*p*-nitrophenylnitramine (15 g.), heated together under reflux for 2½ hr., gave formaldehyde (0·25 g., estimated as dimedone derivative), *N*-methyl-*p*-nitroaniline (9·15 g.), *N*-methyl-2,4-dinitroaniline (0·9 g.), acetophenone (1·5 g.) (2,4-dinitrophenylhydrazone), and tar (1·0 g.).

(e) *In* NN-*diethylaniline.* *N*-Methyl-*N*-*p*-nitrophenylnitramine (15 g.) and diethylaniline (40 c.c.) were boiled together for 2 hr. The solution rapidly darkened and nitric oxide and acetaldehyde (2·4 g.) (2,4-dinitrophenylhydrazone, m. p. 167—168°; dimedone derivative, m. p. 140—141°) were evolved. Steam-distillation removed diethylaniline with some monoethylaniline (toluene-*p*-sulphonyl derivative, m. p. 87·5°). From the material not volatile

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in steam, *N*-methyl-*p*-nitroaniline (6·7 g.) was isolated. The yield of monoethylaniline was 15—20%.

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QUEEN MARY COLLEGE (UNIVERSITY OF LONDON),
LONDON, E.1. [*Received, December 9th*, 1960.]

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514. *Alicyclic Alkoxyl Radicals in the Thermal Decompositions of Cyclohexyl and 1-Methylcyclohexyl Nitrite.*

By PETER GRAY, P. RATHBONE, and A. WILLIAMS.

The thermal decompositions of cyclohexyl and 1-methylcyclohexyl nitrite have been studied in the liquid, gaseous, and dissolved states, at temperatures between 80° and 225°. Decomposition is initiated by fission of the oxygen–nitrogen bond, yielding nitric oxide and the oxygen radical, $C_6H_{10}\!>\!C\!<^{R}_{O\cdot}$ (R = H or Me).

In solvents such as cumene, which contain readily abstractable hydrogen, conversion of the radical into the appropriate alcohol is essentially complete, and decomposition follows first-order kinetics. In inert solvents, in the pure liquid, and in the gaseous phase, decomposition is much more extensive. Only about half the carbon skeleton survives (as the cyclohexanol) and cyclohexanone is not a product. The nitric oxide produced in the initial step participates in several secondary reactions; part is incorporated in an intractable tar and part is reduced to nitrous oxide and nitrogen.

The chemistry of the cyclohexyloxyl radicals is compared with that of other alicyclic and heterocyclic oxygen radicals. Although decomposition might be expected to follow either of two paths it apparently occurs exclusively by ring fission. The thermochemical basis of this behaviour is examined and it is suggested that the alternative path to form cyclohexanone (or another cyclic ketone) and the free radical will occur if it is thermochemically favoured. Behaviour of this kind is to be expected of 1-t-butyl-, 1-allyl-, or 1-benzyl-cyclohexyl nitrite.

STUDIES of the thermal decomposition of a number of simple aliphatic nitrites have shown [1,2] that, in both liquid and gaseous phases, reaction is initiated by oxygen–nitrogen bond fission:

$$\text{(1A)}\quad RR'R''C\cdot O\cdot NO \longrightarrow RR'R''C\cdot O\cdot + NO$$

The same step has been found to account for the thermal decomposition of the aryl-substituted nitrites [3] (of which benzyl nitrite [4] is the simplest), and interest is thus added to these more complex nitrites for the information they give about complex alkoxyl radicals.

When the alkoxyl radical possesses an α-hydrogen atom, the "normal" course of reaction [1] is written:

$$\text{(2A)}\quad RR'CH\cdot O\cdot NO \longrightarrow 0{\cdot}5RR'CO + 0{\cdot}5RR'CH\cdot OH + NO$$

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[1] Steacie, "Atomic and Free Radical Reactions," 2nd edn., Reinhold, New York, 1955.
[2] Gray and Williams, *Chem. Rev.*, 1959, **59**, 239.
[3] Pearson and Rathbone, unpublished work, 1959; Rathbone, Ph.D. Diss., University of Leeds, 1961.
[4] Gray, Rathbone, and Williams, *J.*, 1960, 3932.

the alcohol and carbonyl compound arising by reactions of hydrogen abstraction or disproportionation. This (2A) is an oversimplification for it has been found that [5] considerable decomposition of the alkoxyl radicals generated can also occur; the alkyl radicals so formed associate with nitric oxide, yielding nitroso-compounds [6] or their decomposition products:

(3A) $RR'CH{\cdot}O{\cdot} \longrightarrow R + R'{\cdot}CHO$ and $R' + R{\cdot}CHO$

(4A) R (or R') $+ NO \longrightarrow R{\cdot}NO$ (or $R'{\cdot}NO$), etc.

In addition, reduction of nitric oxide has proved to be commoner than originally thought. In the decomposition of the simplest nitrites, reduction proceeds as far as nitrous oxide; [7,8] in decomposition of the more complex nitrites, nitrogen is formed extensively.[3,4,8,9]

Previous work on the alkyl nitrites has been largely confined to the aliphatic esters. In particular, the alicyclic esters have received very little attention. In 1936, Hunter and Marriot [10] reported (briefly) that cyclohexyl nitrite decomposed spontaneously to adipic acid at room temperature; they did not find the cyclohexanol and cyclohexanone which would arise from reaction (2A). However, their decomposition was carried out with free access to the air. In 1937, Thompson and Dainton [11] reported that photolytic decomposition of cyclohexyl nitrite dissolved in carbon tetrachloride gave a complex mixture.

In 1955, Gowenlock and Trotman [6] pyrolysed a series of nitrites in a flow system in order to prepare nitroso-compounds (by reactions 1A, 3A, and 4A). They were unable to isolate nitroso-compounds from the decomposition products of cyclohexyl or 1-methylcyclohexyl nitrite and they raised doubts about the general resemblances between the cyclohexyl nitrites and other nitrite esters.

So far as the saturated cyclic alkoxyl radicals are concerned, studies on peroxides or hydroperoxides afford some information about 1-methylcyclohexyloxyl [12,13] and 1-phenylcyclohexyloxyl,[14] but essentially none about cyclohexyloxyl itself. Accordingly, we have studied the thermal decompositions of cyclohexyl nitrite and 1-methylcyclohexyl nitrite in the liquid, gaseous, and dissolved states. The aims of the work have been to establish the stoicheiometry of decomposition and to determine whether its initial step is fission of the oxygen–nitrogen bond. Although the occurrence of the initial step (1A) has been proved, its immediate products do not react according to scheme (2A); reduction of nitric oxide is extensive, cyclohexanone is absent, and there is much tarry product. The implications of these results for alicyclic O-radicals may be further illuminated by the study of their thermochemistry.

Experimental

Materials.—Cyclohexanol, cumene, chlorobenzene, and benzaldehyde were purchased from Messrs. B.D.H. Ltd. The benzaldehyde was thoroughly degassed and purified by fractional distillation *in vacuo* before use. Freshly purified cyclohexanol is essential if all traces of cyclohexanone are to be absent.

Cyclohexyl nitrite was prepared by slow addition of freshly purified cyclohexanol (free from cyclohexanone) in sulphuric acid to an ice-cold aqueous solution of sodium nitrite. The crude product was washed successively with saturated sodium chloride solution and dilute sodium hydrogen carbonate solution. It was dried (MgO) and finally distilled in a vacuum. Cyclohexyl nitrite slowly decomposes under ordinary conditions of storage [3,10] (in light with

[5] Adler, Gray, and Pratt, *Chem. and Ind.*, 1955, 1517.
[6] Gowenlock and Trotman, *J.*, 1955, 4190; *J.*, 1956, 1670.
[7] Levy, *J. Amer. Chem. Soc.*, 1956, **78**, 1780; *Ind. Eng. Chem.*, 1956, **48**, 762.
[8] Williams, Ph.D. Diss., University of Leeds, 1959.
[9] Kornblum and Oliveto, *J. Amer. Chem. Soc.*, 1948, **71**, 226.
[10] Hunter and Marriot, *J.*, 1936, 285.
[11] Thompson and Dainton, *Trans. Faraday Soc.*, 1937, **33**, 1546.
[12] Milas and Perry, *J. Amer. Chem. Soc.*, 1946, **68**, 1938.
[13] Hawkins, *J.*, 1950, 2801.
[14] Hey, Stirling, and Williams, *J.*, 1957, 1054.

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access to air), crystals of adipic acid being deposited: it was stored *in vacuo* in the dark, in a trap cooled by liquid nitrogen.

1-Methylcyclohexyl nitrite was prepared in a similar manner to cyclohexyl nitrite, with 1-methylcyclohexanol in place of cyclohexanol; 1-methylcyclohexanol was prepared by the action of methylmagnesium iodide on cyclohexanone.

As infrared and ultraviolet spectra of pure liquid cyclohexyl and 1-methylcyclohexyl nitrite are not fully documented, we record here their salient features for comparison with other nitrites.[15] The infrared absorption spectra of thin films were recorded on a Grubb–Parsons double-beam recording infrared spectrometer. Ultraviolet spectra of solutions in cumene and light petroleum were recorded on an Optica double-beam absorption spectrometer.

Infrared absorption spectra: wavelengths in μ (and relative intensities). Cyclohexyl nitrite: 3·45s, 3·50s, 6·11vs, 6·26m, 6·84m, infl., 6·90s, 7·33m, 7·50w, 7·61vw, 7·93w, 7·98vw, 8·37vw, 8·64w, 8·83vw, 9·15vw, 9·44m, 9·76m, 10·26m, 10·56m, 10·70vw, 10·83vw, 11·11s, 11·46w, 11·56m, 11·74vw, 12·13vs, 12·94vs, 14·75s. 1-Methyl cyclohexyl nitrite: 3·41s, 3·47s, 6·14vs, 6·90m, 7·25w, 7·30w, 7·45vw, 7·51vw, 7·81vw, 7·95vw, 8·00w, 8·59m, 8·67m, 8·97w, 10·29w, 10·62m, 11·03vw, 11·11vw, 11·20vw, 11·68w, 11·83w, 12·13s, 12·7vs, 13·31s.

Ultraviolet spectra: wavelengths in mμ (extinction coefficients, ε, in parentheses). Cyclohexyl nitrite in light petroleum: 324 (24), 334 (36), 345 (54), 358 (72), 371 (71), 385 (infl., 42).

1-Methylcyclohexyl nitrite in the same solvent: 331 (24), 342 (35), 354 (54), 367 (76), 382 (82), 399 (56).

Procedure for Liquid-phase Decomposition.—The liquid-phase decompositions were carried out in the apparatus [4] used for the decomposition of liquid benzyl nitrite. A weighed sample of reactants in a Pyrex reaction vessel was carefully freed from dissolved air. The inert gaseous atmosphere (nitrogen or carbon dioxide) was then admitted.

The reaction vessel was maintained at a constant temperature by the vapour of a boiling liquid. In some experiments the progress of the decomposition was followed by measurement of the gas evolution.

Procedure for Gas-phase Decomposition.—The gas-phase decomposition of cyclohexyl nitrite was studied in both a static and a flow system.

In the static system a Pyrex reaction vessel (volume *ca.* 80 ml.) was connected to a conventional vacuum-line. The reaction bulb was heated to the required temperature (*ca.* 200°) by means of an easily removable furnace. The pressure in the reaction vessel was measured by a heated capillary manometer. Cyclohexyl nitrite was distilled into the cold reaction vessel. The furnace was replaced in position and heated to 120°; the (initial) pressure at this temperature was taken. To study the decomposition, the furnace at 120° was quickly replaced by one at the required temperature. The condensable products were distilled into a small trap which was removed for the products to be analysed. The gaseous products were expanded into an infrared cell.

In the flow apparatus, a Pyrex reaction vessel (44 ml.) was kept at *ca.* 250° by means of an electric furnace. The nitrite vapour was carried through the reaction vessel (mean residence times *ca.* 10 sec.) by a stream of nitrogen at atmospheric pressure and the decomposition products were collected in a trap cooled to −78°. Samples of the gas were removed for infrared analysis.

Analysis of Gaseous Products.—The gaseous products (A) of decomposition of both nitrites contain nitrogen, nitric oxide, and nitrous oxide together with a small quantity of carbon dioxide; no carbon monoxide was detected. Similar analytical methods were applicable to the products of both gas and liquid-phase decompositions. Nitric and nitrous oxides and carbon dioxide were estimated quantitatively from infrared absorption spectra (maxima at 5·2, 4·5, and 4·3 μ, respectively). Nitrogen was determined by measuring the residual pressure when nitric and nitrous oxide and carbon dioxide were condensed out.

Analysis of Liquid Products.—The non-gaseous part (B) of the decomposition products is a dark, viscous liquid. Distillation yields a clear distillate (C) and an almost equal amount of an involatile oily residue (D).

The distillate (C) is almost wholly the appropriate cyclohexanol: other constituents were separated by fractionation and identified by ultraviolet and infrared spectroscopy, by vapour-phase chromatography, and by chemical or other physical tests where applicable.

Cyclohexanol was determined by both fractionation and weighing, and by comparison of

[15] Bellamy, " The Infrared Spectra of Complex Molecules," 2nd edn., Methuen, London, 1958.

its infrared spectrum in cumene solution (especially the peak at 2·65 μ) with those of standard solutions. In addition to cyclohexanol, water was found in small quantities in the volatile fraction (C); cyclohexene was identified as a very small fraction (b. p. 83°/760 mm.; decolorises bromine water). An aldehyde was detected by dimedone: a deep orange 2,4-dinitrophenylhydrazone, m. p. 135—140°, was prepared but not conclusively identified.

Element analysis of the oily residue (D) showed it to contain a considerable percentage of nitrogen; it was also acidic. The acidic component (possibly adipic acid) was estimated quantitatively by titration against standard sodium hydroxide.

Cyclohexanone was not present among the liquid products of normal decomposition of either pure nitrite. In the experiments on the influence of initially added cyclohexanone, the residual quantity was determined by comparing the vapour-phase chromatogram with that of standard comparison mixtures of similar composition. This proved more accurate than a gravimetric assay with 2,4-dinitrophenylhydrazine.

Results

Decomposition of Cyclohexyl Nitrite in the Gas Phase.—Decomposition is slower in the gas phase than in the pure liquid, less than 2% of reaction occurring after 4 hr. at 100°. At higher temperatures, reaction is more rapid and may be followed analytically or by pressure measurements, the pressure increase accompanying complete decomposition being 50%. The gas-phase decomposition was studied in outline only; some product analyses are included in Table 1.

In the " static " apparatus at 224°, reaction is essentially complete in 30 min. The gases formed comprise (as 100 mole % of nitrite): NO 28·6; N_2 7; N_2O 2·6; the volatile liquids are water (*ca.* 10 mole %) and cyclohexanol (*ca.* 20 mole %); cyclohexanone is absent. A black tarry residue (41·4 g. per mole) remains in the reaction vessel after decomposition.

In a " flow " apparatus it is possible to handle larger amounts of reactants. The non-gaseous product of pyrolysis at 250° in a stream of nitrogen gas (contact time *ca.* 10 sec.) is again a

Table 1. *Decomposition products of liquid and gaseous cyclohexyl nitrite. Yields are expressed as mole % of initial nitrite.*

Conditions	Temp.	Decompn. hr.	Decompn. min.	Cyclo-hexanol	Adipic acid	NO	N_2O	N_2	CO_2	Gas, total
Liquid-phase	100°	18	—	45	5					
decomp.	132	1	40	—	—	8·2	5·2	13	1·9	28
		3	55	50	4·1	11	10·5	17	3·1	42
		4	45	—	—	—	—	18	—	42
		6	40	—	—	10	10	16	3·9	40
	132	2	32		39 *	3·5	23	11	1·1	40
Gas.-phase	224	—	30	20	10 †	28·6	2·6	7·0	Trace	38
decomp.	250	—	(10 sec.)			30	3	*ca.* 15	Trace	*ca.* 48

* Equivs. of adipic plus benzoic acid; this run was carried out in presence of added benzaldehyde.
† Water.

dark, viscous liquid containing, in addition to the cyclohexanol and water (the main constituents), aliphatic aldehydes and showing infrared absorption bands at 6·13 7·25, 7·95, 9·4, and 10·85 μ ascribed to *C*-nitroso-derivatives or oximes.

Decomposition of Pure Liquid Cyclohexyl Nitrite.—The stoicheiometry and kinetics of decomposition (carried out under an inert atmosphere to prevent atmospheric oxidation) of liquid cyclohexyl nitrite have been studied at 100° and 132°.

Stoicheiometry. The products of decomposition are a gas (A) and a dark, viscous liquid (B). The gas is a mixture of nitrogen, nitrous oxide, nitric oxide, and a little carbon dioxide; the total yield of gas at 132° is 0·42 mole per mole of nitrite; about 64% of the total nitrogen is accounted for by the gaseous constituents: N_2O 0·17, N_2 0·10, and NO 0·10 mole (cf. Table 1). The proportions of nitrous oxide and carbon dioxide in the gaseous products increase somewhat as reaction proceeds.

The non-gaseous fraction (B) was examined before and after fractionation. The principal identifiable constituent is cyclohexanol; cyclohexanone is absent. Fractionation yielded cyclohexene (b. p. 83°), a trace; water (b. p. 100°); cyclohexanol (b. p. 161°); and 60 g. per mole of nitrite of a black oil (D) (C, 63·45; H, 8·0; N, 5·7%). This (D) contained the adipic

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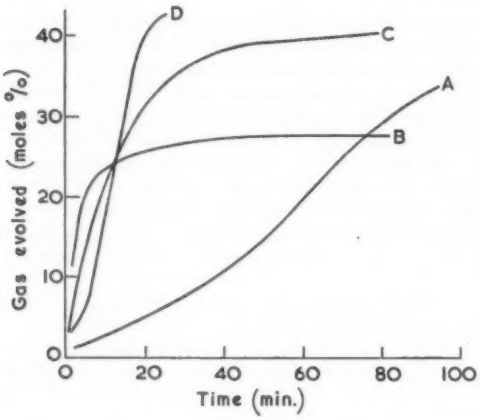
acid fraction; titration corresponded to 0·08 equiv. per mole of nitrite. It was fractionated with difficulty *in vacuo*, to yield a black liquid (E), b. p. >250°, and 19 g. of a black solid (F). The liquid (E) contained both carbonyl groups (strong infrared absorption at 5·81 μ) not attributable to cyclohexanone (b. p. 155°) and nitroso-groups. It was thought to be a nitroso-cyclohexanone derivative. The evidence is, however, inconclusive, and the appropriate reference compounds are unknown. Infrared spectra of material (D) also demonstrated the absence of hydroxyl groups, and therefore the oxygen is probably present as carbonyl and nitroso-groups.

The course of decomposition may be represented by the equation:

$$1{\cdot}00C_6H_{11}{\cdot}O{\cdot}NO \longrightarrow 0{\cdot}45C_6H_{11}{\cdot}OH + 0{\cdot}17N_2 + 0{\cdot}14H_2O + 0{\cdot}11NO + 0{\cdot}10N_2O + 0{\cdot}04C_6H_{10}O_4 + 0{\cdot}035CO_2 + C_{3{\cdot}03}H_{4{\cdot}92}N_{0{\cdot}35}O_{0{\cdot}27}$$

That cyclohexanone is not present implies that it is not formed at all, or that it is formed but consumed. A solution containing cyclohexanone and cyclohexyl nitrite (molecular ratio



The kinetic course of decomposition of liquid cyclohexyl nitrite at 132°. *Autocatalysis and the influence of added cyclohexanone.* (*Ordinates are moles of gas evolved per* 100 *moles of initial nitrite; abscissae are elapsed time, in minutes.*)

A, Pure nitrite (mean of three runs); B, Added cyclohexanone (50% ketone); C, Added cyclohexanone (33% ketone); D, Added benzaldehyde (33% nitrite).

1 : 2) was kept at 132° for 12 hr. One half of the added cyclohexanone was still present at the end of this period.

Kinetics.—After 4 hr. at 100°, the liquid had become brown; infrared spectroscopy revealed that nitrite had been consumed and that hydroxyl groups had been formed. After complete decomposition the residue was black. At 132°, decomposition was essentially complete in less than 3 hr. Though the complex stoicheiometry prevents more than a superficial analysis, the progress of decomposition can be followed quantitatively by measurements of evolved gas or consumed nitrite. The Figure displays the amount of gas evolved at 132° in moles per 100 moles of initial nitrite as a function of time. One feature stands out: decomposition of the pure liquid is autocatalytic.

To investigate whether cyclohexanone might be a catalyst (as benzaldehyde is for decomposition of benzyl nitrite [4]) the decompositions of mixtures of cyclohexyl nitrite with equi- and semi-molecular proportions of added cyclohexanone were studied. The rate of reaction was considerably increased, and cyclohexanone is potentially the autocatalytic agent. The effect is not specific, however, for added benzaldehyde brings about the same result.

Decomposition of Cyclohexyl Nitrite in Cumene.—To discover if the cyclohexyloxyl radical $C_6H_{11}{\cdot}O{\cdot}$ is formed during decomposition, solutions of cyclohexyl nitrite in cumene were decomposed at 100° and 132° and the yields of cyclohexanol determined. At 132°, reaction was complete in a few hours. The final solutions were deep red-brown and this colour was retained in the last 1% of the involatile fraction when the liquid product was fractionated *in vacuo*.

The yield of cyclohexanol (see Table 2) was high, increasing from 90 to 97% as the solvent : nitrite ratio was increased. Bi-α-cumyl was not found.

The kinetic course of hydrogen-abstraction was examined in outline by determining the

TABLE 2. *Formation of cyclohexyloxyl radicals in the decompositions of cyclohexyl and 1-methylcyclohexyl nitrites. The figures are yields of alcohol from decomposition in cumene at* 132° (*run* 18 *at* 100°).

Run	Nitrite	Initial nitrite concn. (mole $l.^{-1}$)	Duration (hr.)	Moles of alcohol per 100 moles of initial nitrite
9	Cyclohexyl	0·172	12	91
10		0·0980	8	95
11		0·0510	9	97
18		0·0741	6	95
22	1-Methylcyclohexyl	0·149	14	70
23		0·0507	12	90

yield of alcohol at intervals. 100 g. of a 0·07408m-solution were kept at 100°; the following yields were recorded:

Time (min.)	0	135	285	720
Yield (%) of alcohol	0	50	81	95

These figures are in accord with a first-order reaction velocity constant, $k = 1{\cdot}7 \times 10^{-5}$ $sec.^{-1}$ at 100°.

Decomposition of Cyclohexyl Nitrite in Chlorobenzene.—Unlike cumene, chlorobenzene contains no readily extractable hydrogen. Since hydrogen abstraction leading to cyclohexanol is a competitor of decomposition by ring fission, chlorobenzene should favour the latter by removing the opportunities for the former.

TABLE 3. *Decomposition of cyclohexyl and 1-methylcyclohexyl nitrite in chlorobenzene at* 132°. *Figures are yields of alcohol expressed in terms of moles per* 100 *moles of initial nitrite.*

Run	Nitrite	Initial nitrite concn. (mole $l.^{-1}$)	Decompn. time (hr.)	Alcohol yield
27	Cyclohexyl	0·082	36	52
28	,,	0·0137	24	55
12	1-Methylcyclohexyl	0·038	43	54
13	,, ,,	0·076	30	59

Solutions containing about 0·3 g. of cyclohexyl nitrite in 10 ml. of chlorobenzene were heated at 100° for 18 hr. Cyclohexanol yields, determined by infrared analysis, are summarised in Table 3. They were much less than yields in cumene, and about the same as those obtained in the pure liquid.

An exploratory investigation of the other decomposition products was consistent with the presence of aliphatic aldehydes and *C*-nitroso-groups. The former were suggested by infrared spectra (5·78 μ) and by a dimedone test; the latter by infrared (6·9 μ) and ultraviolet (264, 272, 276 mμ) absorption maxima (in hexachloroethane and ethanol respectively).

Decomposition of Pure Liquid 1-Methylcyclohexyl Nitrite.—1-Methylcyclohexyl nitrite is considerably more stable than is cyclohexyl nitrite, though it also decomposes in the air at room temperature, eventually yielding a crystalline acid.

TABLE 4. *Analysis of decomposition products of pure liquid 1-methylcyclohexyl nitrite at* 132°. *Figures are yields expressed in moles per* 100 *moles of initial nitrite.*

Decompn. time hr.	min.	C_7H_{14}·OH	NO	N_2O	N_2	CO_2	Gas, total
8	40	64	8·9	4·8	21	5·7	41
18	30	—	9·1	3·5	22	3·8	39

Under a nitrogen atmosphere decomposition occurs conveniently rapidly at 132°. It was accompanied by darkening, and the viscous liquid finally produced was almost black. The gaseous products were nitric oxide, nitrogen, nitrous oxide, and carbon dioxide. Among the liquids, only 1-methylcyclohexanol was prominent. A small quantity of a ketone was indicated by the infrared spectrum and by the formation of a small quantity of a deep orange 2,4-dinitrophenylhydrazone; a negative iodoform test suggested that it was not a methyl ketone. Element

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analyses were made on the volatile and involatile fractions of the non-gaseous products. The volatile fraction contained: C, 70·3; H, 11·95; N, 1·55; and O, 16·2%. The tarry residue contained much more nitrogen: C, 59·75; H, 7·55; N, 8·05; and O, 24·65%). Table 3 summarises the results, which may be represented by the overall scheme:

$$1{\cdot}00C_7H_{13}{\cdot}O{\cdot}NO\ (144{\cdot}2\ g.) \longrightarrow 0{\cdot}64C_7H_{13}{\cdot}OH + 0{\cdot}21N_2 + 0{\cdot}09NO + 0{\cdot}05CO_2 + 0{\cdot}04N_2O + Tar\ (43\ g.)$$

The rate of decomposition is somewhat irreproducible but autocatalysis is again present. In one run at 132°, reaction proceeded slowly for *ca.* 7 hr., then accelerated sufficiently to be essentially complete after 8 hr. 30 min.

Decomposition of 1-*Methylcyclohexyl Nitrite in Cumene.*—Solutions in cumene containing 0·149 and 0·507 mole of 1-methylcyclohexyl nitrite per l. were decomposed essentially to completion at 132°, and yields of alcohol determined. The results are summarised in Table 2. The yield was higher (*ca.* 90%) in the more dilute solution. Bi-α-cumyl was not found.

Decomposition of 1-*Methylcyclohexyl Nitrite in Chlorobenzene.*—Solutions in chlorobenzene containing 0·08 and 0·04 mole of 1-methylcyclohexyl nitrite per l. were decomposed to completion at 132°. Yields of 1-methylcyclohexanol were determined: the results are presented in Table 3. Alcohol yields (*ca.* 59% and 55%) are reduced from those obtained in cumene solution to values similar to those obtained in the pure liquid (*ca.* 65 moles %).

Discussion

Formation of the Alkoxyl Radical.—The nature of the initial step in the thermal decomposition of these nitrites is revealed by the results obtained when decomposition is carried out in cumene. The alcohol yields rise to 100% in dilute solution. That this is a true chemical effect and not merely a physical consequence of dilution is proved by the much lower alcohol yields formed when decomposition is carried out in the inert solvent, chlorobenzene. The alcohol results from attack by the alkoxyl radical on the weakly bound tertiary hydrogen atom of cumene. Reaction is thus initiated by unimolecular oxygen–nitrogen bond fission to yield nitric oxide and the appropriate cyclohexyloxyl radical:

These cyclic nitrites thus fall into line with other members of the family and, although

$$RO{\cdot}NO \longrightarrow RO{\cdot} + {\cdot}NO$$
$$RO{\cdot} + PhMe_2CH \longrightarrow ROH + PhMe_2C{\cdot}$$
(R = cyclohexyl or 1-methylcyclohexyl)

previously attention has been drawn [6] to differences from other nitrites, these refer to subsequent reactions of the radicals and not to the initial step. The formation of a little cyclohexene may be evidence for the concurrent elimination: $C_6H_{11}{\cdot}O{\cdot}NO \longrightarrow C_6H_{10} + HO{\cdot}NO$. There is strong evidence for this in the isomeric family of nitroparaffins though it has not hitherto been reported for nitrites. The extent is very slight.

Bi-α-cumyl is not found as a product. The same absence of bicumyl has been noted (or its presence not reported [16]) in the decompositions in cumene solution of benzyl nitrite [4] and t-butyl nitrite; [16] it also has a parallel [17] in the absence of bibenzyl from the products of decomposition in toluene solution of n-octyl nitrite. Waters [18] has suggested that an alternative fate of the cumyl radical is oxidation to α-methylstyrene (b. p. 161°) by loss of hydrogen and that the stoicheiometry of hydrogen abstraction from cumene by alkoxyl radicals is the sum of the reactions:

$$RO{\cdot} + PhMe_2CH \longrightarrow ROH + PhMe_2C{\cdot}$$
$$X{\cdot} + PhMe_2C{\cdot} \longrightarrow XH + PhMeC{=}CH_2 \quad (X \text{ may be RO})$$
$$2RO{\cdot} + PhMe_2CH \longrightarrow 2ROH + PhMeC{=}CH_2$$

In nitrite systems, nitric oxide also may take the rôle assigned to X, but in addition it may associate with cumyl radicals yielding a nitroso-compound.

[16] Yoffe, *Research*, 1954, **7**, 44.
[17] Gingras and Waters, *J.*, 1954, 3508.
[18] Waters, personal communication, 1960.

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As we pass from decompositions in dilute cumene solution to decomposition in the pure liquid or gas phase, the stoicheiometry alters; three features of the general pattern stand out. First, yields of alcohol fall to about 50% and this figure accounts for most of the intact cyclohexyl rings. Secondly, cyclohexanone is absent from both systems. Thirdly, there is considerable reduction of nitric oxide to nitrous oxide and nitrogen, and, although commonly [2,4,7] these gaseous constituents comprise all the nitrogen products, more than 35% of the total nitrogen here ends in the involatile tar. These are the observations to be explained in terms of reactions undergone by the nitric oxide and the alkoxyl radicals formed in the initial step.

Hydrogen-abstraction Reactions.—Hydrogen abstraction by the alkoxyl radicals is the origin of the two cyclohexanols. The substrates available are the parent nitrite, another alkoxyl radical (*i.e.*, disproportionation), and a product molecule. Although cyclohexyl nitrite (the ester of a secondary alcohol) offers a readily abstractable atom in its α-hydrogen, it is not exclusively this atom which is attacked here, for, if it were, cyclohexanone would be a major product. The possibility that some cyclohexanone is formed but is consumed in secondary reactions cannot be completely ruled out. It is reactive; cyclohexanone is readily oxidised by homolytic attack, much more so than is cyclohexanol; [15] and it can undergo [15] acid-catalysed condensation to β-unsaturated ketones. However, the survival of a considerable portion of initially added cyclohexanone and its complete absence on normal decomposition confirm that, if there is attack on this position, its extent is small.

Therefore, hydrogen abstraction is occurring (concurrently) from another position in the ring. All the hydrogen atoms of the cyclohexyl ring are relatively labile; even from cyclohexane itself, hydrogen abstraction by t-butoxyl [19] proceeds more readily than from isoparaffins, and at 135° is favoured even relatively to cumene. The activation energy of hydrogen abstraction by t-butoxyl from methylcyclohexane is only *ca.* 6 kcal. mole^{-1}. Hydrogen abstraction [20] from the methylene groups of cyclohexanone leads to higher ketones and to dicyclic 1,4-diketones.

Moreover, in the decomposition of 1-methylcyclohexyl nitrite the yield of 1-methylcyclohexanol is no less than that of cyclohexanol from cyclohexyl nitrite; since 1-methylcyclohexyl nitrite does not possess any α-hydrogen, abstraction must there occur exclusively from elsewhere in the ring. The work of Hawkins,[13] which records the formation of 1-methylcyclohexanol in the decomposition of 1-methylcyclohexyl hydroperoxide, also requires this conclusion.

This behaviour contrasts with that observed in systems involving the cyclohexenyloxyl [21] and tetrahydropyranyloxyl [22] radicals. These yield considerable proportions of the parent alcohols and ketones, whether by disporportionation or attack on the parent. In each there is both the presence of an exceptionally weakly bound α-hydrogen atom and the possibility of an unusually stable ketone. The two factors owe their origin in the homocyclic system to the allylic configuration, and in the heterocyclic system to the influence of the oxygen atom.

Decomposition of the Alkoxyl Radicals and Reactions of the Nitric Oxide.—Radical decomposition is the normal competitor [2] of hydrogen abstraction and is the fate of nearly half the cyclic alkoxyl radicals produced here. Fission of the carbon–carbon bond in a cyclic alkoxyl radical (I) produces not separate fragments (*i.e.*, path b is not followed), but a single species (II) containing both carbonyl and alkyl radical groups (path a).[2] It is most striking that unimolecular decomposition by elimination of the group R leaving cyclohexanone (path b) has never been recorded In agreement with this general observation no methane, ethane, or nitrosomethane was formed from 1-methylcyclohexyl nitrite in our work. This step is the first on the path leading to aldehydic, ketonic, and acidic

[19] Brook, *Trans. Faraday Soc.*, 1957, **53**, 327.
[20] Farmer and Moore, *J.*, 1951, 131.
[21] Bateman and Hughes, *J.*, 1952, 4594.
[22] Milas, Peeler, and Mageli, *J. Amer. Chem. Soc.*, 1954, **76**, 2322.

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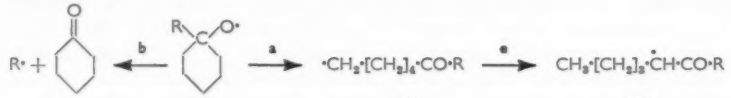
products and to the polymeric, tarry residues characteristic [12-14] of alicyclic oxygen radical decompositions.



(I) (II) (III)

In the absence of nitric oxide, the radical (II) may react in three ways: (path c) it may abstract a hydrogen atom forming hexanal (when R = H) or heptan-2-one [12] (when R = Me); (path d) it may dimerise to a 1,12-dialdehyde (R = H) or diketone [12] (R = Me); or (path e) it may rearrange by an internal hydrogen abstraction. Rearrangement of the radical (II; R = Me) to (III) has been recognised in the decomposition [12] of t-butyl 1-methylcyclohexyl peroxide, 3,4-dibutylhexane-2,5-dione being the end-product of dimerisation of (III), and 3-methylheptan-2-one the end-product of association of (III) with methyl radicals from t-butoxyl.

In these nitrite decompositions, about 40% of the rings are ruptured in this way. The radical (II; R = H) is also the source of the adipic acid in decomposition of cyclohexyl nitrite:

$$\cdot CH_2\cdot[CH_2]_4\cdot CHO \xrightarrow{\text{Oxid.}} HO_2C\cdot[CH_2]_4\cdot CO_2H$$

In nitrite pyrolyses, formation of nitroso-compounds is well established [6,16] as another consequence of the decomposition [5] of an alkoxyl radical, the alkyl radical eliminated associating with nitric oxide. The same association here leads probably through nitroso-aldehydes and nitroso-ketones to complex decomposition products. The intractable tarry residues, characteristic of all cyclic alkoxyl radical decompositions,[12-14] are now further complicated by nitrogenous constituents. There is evidence for carbon–nitrogen bond formation (and for the presence of nitroso-groups), and Williams [8] has pointed out that the composition of the solid component of the tar * corresponds to an empirical formula near that of a C_6-nitroso-aldehyde.

The reduction of the nitric oxide which remains in the gas phase is also marked; about 50% ends as nitrous oxide and nitrogen. These figures are also in accord with the generalisation [4,23] that, though reduction of nitric oxide always occurs in pyrolyses of nitrites, yet with the simpler nitrites [23] it rarely proceeds beyond nitrous oxide while with the higher nitrites [3,4,8,9] nitrogen is formed and often predominates. The mechanism is by no means understood. The species HNO, formed [7] in a hydrogen-abstraction reaction by nitric oxide, is the most probable precursor of nitrous oxide. However, whether nitrogen in turn is wholly formed from nitrous oxide or whether there is a direct path [24] from nitric oxide to nitrogen is not known.

Energy Requirements of Ring Fission.—The strong preference for ring fission as against radical elimination is not confined to 6-membered rings with these simple substituents. Thus, 1-phenylcyclohexyloxyl radicals [14] split in the same way, forming pentyl phenyl ketone (37%) and 1,10-dibenzoyldecane (but not cyclohexanone and benzene). The original investigators [14] ascribed this preferential cleavage to the superior stability of the ketonic product originating in the conjugation of its carbonyl and phenyl groups. Although this is a contributory [25] factor, it is not a necessary one, since the same path is pursued when R = H, OH, or Me [12] as when R = Ph.

* A Referee has suggested that a polymer $-[-\overset{|}{C}-\overset{|}{C}=N-O-]_n-$ could be formed by the polymerisation as a diene of a nitroso-compound of basic structure $\overset{|}{C}=\overset{|}{C}-N=O$.

[23] Gray and Williams, *Nature*, 1960, **188**, 56; Eighth (International) Symposium on Combustion, Pasadena, 1960, in the press.
[24] Donaruma and Carmody, *J. Org. Chem.*, 1957, **22**, 635.
[25] Gray and Williams, *Trans. Faraday Soc.*, 1959, **55**, 760.

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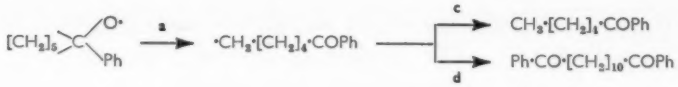

The same pattern is found in the hydroaromatic series: 1-tetralyloxyl,[27] 9-decalyloxyl,[28] and the tricyclic pinanoxyl [29] follow the same path. Among the five-membered rings, alkoxyl radicals have been examined [26] with R = Me, OMe, or OH, and the corresponding dimerised products of the initially ruptured ring have been found, often in high yield. The hydroxy- and methoxy-substituted radicals dimerise to dibasic acids and their methyl esters, respectively.

Some light is thrown on the preferential ring fission by an examination of the thermochemistry.[2,25] Table 5 summarises the enthalpies of unimolecular decomposition (strictly,

TABLE 5. *Energy requirements of ring fission and radical (or atom) elimination from cyclic alkoxyl radicals (6-membered rings).*

Parent alkoxyl	Group eliminated	Carbonyl compound	ΔH (kcal. mole^{-1})
Cyclohexyloxyl	H	Cyclohexanone	16
	Ring fission	·CH$_2$·[CH$_2$]$_4$·CHO	0
1-Methylcyclohexyloxyl	Me	Cyclohexanone	4
	Ring fission	·CH$_2$·[CH$_2$]$_4$·COMe	2
1-Phenylcyclohexyloxyl	Ph	Cyclohexanone	9
	Ring fission	·CH$_2$·[CH$_2$]$_4$·COPh	2
1-t-Butylcyclohexyloxyl	Bu^t	Cyclohexanone	−5
	Ring fission	·CH$_2$·[CH$_2$]$_4$·COBu^t	+1·5
Decalyl-9-oxyl	1–9 Ring fission	Monocyclic radical	−1
	9–10 Ring fission	Monocyclic radical	0
Cyclohex-1-enyl hydroperoxide	H	Cyclohex-1-enone	−3
	Ring fission	·CH$_2$·[CH$_2$]$_2$·CH=CH·CHO	1
1-Hydroxycyclohexyloxyl	HO	Cyclohexanone	20
	Ring fission	·CH$_2$·[CH$_2$]$_2$·CH=CH·CHO	1
Tetrahydropyranyl-1-oxyl	H	Tetrahydro-1-oxopyran	16
	Ring fission	·CH$_2$·[CH$_2$]$_3$·O·CHO	0

in the gaseous phase) of some homocyclic alkoxyl radicals by the alternative paths available. Removing the hydrogen atom needs 16 kcal. mole^{-1}; removing the phenyl group, 9 kcal. mole^{-1}; removing the methyl group, 4 kcal. mole^{-1}. The difference between methyl and phenyl may be attributed to the conjugation in the products as suggested by Hey *et al.*[14]

In every case, ring fission required less energy than radical loss, and once again the kinetic features of reactivity have a reflection in the thermodynamic aspect. The extension of this principle suggests [25] that the alternative path (a) to liberate the radical and leave the cyclic ketone will occur when it is thermochemically favourable. On this basis, radical elimination and cyclohexanone formation are to be expected in the decomposition of the substituted cyclohexyloxyl derivatives 1-R·C$_6$H$_{10}$·O· where R is, *e.g.*, t-butyl (see Table 5), allyl, or benzyl.

We express our warmest thanks to Drs. K. J. Ivin and M. W. T. Pratt for many valuable discussions, to Mr. M. J. Pearson for help with some of the experiments on cyclohexyl nitrite decomposition, and to Professor D. H. Hey and Dr. W. A. Waters for numerous useful comments. We are also grateful to the Merthyr Tydfil Education Committee and to the D.S.I.R. for postgraduate awards to A. W. and P. R. respectively.

SCHOOL OF CHEMISTRY,
THE UNIVERSITY, LEEDS, 2. [*Received, January 24th*, 1961.]

[26] Roedel, U.S.P. 2,601,224/1952; *Chem. Abs.*, 1953, **47**, 4363.
[27] Robertson and Waters, *Trans. Faraday Soc.*, 1946, **42**, 201; *J.*, 1948, 1574, 1578, 1585.
[28] Holmquist, Rothrock, Theobald, and Englund, *J. Amer. Chem. Soc.*, 1956, **78**, 5339.
[29] Schmidt and Fisher, *J. Amer. Chem. Soc.*, 1954, **76**, 5426.

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515. *Diffusional Band-spreading in Gas-chromatographic Columns. Part II.*[1] *The Elution of Sorbed Vapours.*

By J. Bohemen and J. H. Purnell.

The elution of acetone and benzene vapour by hydrogen and nitrogen from columns differing in the particle size of the solid supports has been studied. The results are interpreted in terms of a rate equation with four constants and three variables. The evidence suggests that the labyrinth constant γ is probably unity and that the tortuosity constant λ is about 1·5. The need for a Golay-type term for the resistance to mass-transfer of gas in the rate equation for packed columns has been substantiated. A value of the proportionating constant has been deduced to modify the term, as theoretically deduced for uniform capillaries, for use with packed columns. The results indicate that the distribution of involatile solvent is of the droplet and not of the film type. The significance of the results in relation to high-speed chromatography is briefly discussed.

In Part I [1] of this work the chromatographic rate equation of van Deemter *et al.*[2] was modified so as to include a term for the mass-transfer of gas and corrections for the pressure-dependence of the various terms. It was shown that the theoretical plate height, H, and the linear inter-particle velocity (u_0) of the carrier gas at the column outlet-pressure (p_0) (recalculated to the value it would have at one atmosphere pressure, u') are related by the equation

$$H = A + B'/u' + C_g'u' + (C_lu'f)/p_0. \quad (1)$$

A and B' were defined earlier;[1] f is the pressure compressibility correction function of James and Martin.[3] An equation defining C_g' in terms of experimental quantities has been developed by Golay [4] for the particular case of uniform capillary columns. It is assumed here that Golay's theory is applicable to packed columns since, for theoretical purposes, these are usually regarded as bundles of non-uniform capillaries. For a packed column it is supposed that Golay's coefficient can be written

$$C_g' = \frac{\chi[1 + 6k' + 11(k')^2]d_p^2}{24(1 + k')^2 D_g'}, \quad (2)$$

where $k' = KV_l/V_d$; K represents a partition coefficient, V_l the volume of solvent in a column, and V_d the total free gas space in the column (inter- + intra-particle). D_g' is the interdiffusion coefficient of the solute in the carrier gas at 1 atm. and at the column temperature while χ is a proportionating constant. In practice k' is the ratio of the true retention volumes of any solute and an inert gas. The expression for the liquid mass-transfer coefficient, C_l, deduced by van Deemter *et al.*,[2] is

$$C_l = \frac{2k'd_f^2}{3(1 + k')^2 D_l}, \quad (3)$$

where d_f is a representative solvent-film thickness and D_l is the interdiffusion coefficient of the solute in the stationary liquid in the conditions employed.

The application to experiment of the original van Deemter equation, which does not include the C_g' term, has been described by several investigators.[5-9] The results have

[1] Part I, Bohemen and Purnell, *J.*, 1961, 360.
[2] van Deemter, Zuiderweg, and Klinkenberg, *Chem. Eng. Sci.*, 1956, **5**, 271.
[3] James and Martin, *Biochem. J.*, 1952, **50**, 679.
[4] Golay in "Gas Chromatography" (ed. D. H. Desty), 1958, Butterworths, London, p. 36.
[5] Scott, as in ref. 4, p. 189.
[6] Keulemans and Kwantes, "Vapour Phase Chromatography" (ed. D. H. Desty), 1957, Butterworths, London, p. 15.
[7] Bohemen and Purnell, as in ref. 4, p. 6.
[8] Purnell, *Ann. New York Acad. Sci.*, 1959, **72**, 592.
[9] Desty, Godfrey, and Harbourn, as in ref. 4, p. 200; de Wet and Pretorius, *Analyt. Chem.*, 1948, **30**, 325; Brennan and Kemball, *J. Inst. Petroleum*, 1958, **44**, 14.

usually shown qualitative agreement with the theory, but the quantitative data and evaluated coefficients of different workers are rarely concordant. The reasons are almost certainly failure to take account of extra-column processes, inappropriate methods of evaluating the coefficients, the use of gas velocities which are wrongly calculated, and the failure to introduce the Golay term. Elucidation of the true individual term contributions to the total value of H is important both from the theoretical standpoint and in attempts to obtain greater column efficiency [5,7,8] and speeds of analysis.[10] The work now described was carried out in order to obtain more reliable quantitative information about column performance and to determine whether or not the use of equation (1) would provide more consistent data with which to test the theory. The latter seemed likely since the equation has been shown [1] to be successful for the elution of unsorbed gases.

It was considered essential first to ensure that, so far as possible, extra-column processes, which are not accounted for in equation (1), contributed nothing to the results. Of these, the effects of sample size,[3,6,7,11,12] sample composition,[3,7,13] and anomalous katharometric response [14] have been studied in some detail and were not re-investigated. Other possible sources of band-broadening, however, such as excessive volume of sample feed and adsorption by solid supports, have received less attention and were thought to merit study.

Experimental

The apparatus and columns used were those described previously,[1] with inclusion of a needle valve and pressure gauge at the column outlet to allow column operation at elevated outlet-pressures. Nitrogen and hydrogen were used as carrier gases, and columns were controlled at 51° in all the experiments. The volume and band shape of the sample after injection, but immediately before entering the chromatographic column, were determined by passing the sample through one side of a twin-cell katharometer situated at the column head. An injection peak thus appeared on the chromatogram.

In the experiments relating to extra-column processes, 4-μl. liquid samples containing cyclohexane, acetone, benzene, and propan-2-ol in the ratio 0·3 : 0·7 : 1·0 : 4·6 were used, the propan-2-ol acting primarily as a diluent. These samples were injected into the carrier-gas stream through a rubber septum with an Agla micrometer syringe.[15] In the study of the column band-spreading processes, 1-μl. liquid samples of cyclohexane, acetone, and benzene in the ratio 0·3 : 0·7 : 1·0 were used. These were injected into the column by means of an O-ring rotary-valve system [1] used in conjuction with a modified Agla syringe.[16] The injection temperature for both injection methods was adjusted so that a further increase in temperature did not reduce the widths of the elution curves,[17] this temperature being about 130°.

Results and Discussion

The Sample Feed Volume.—The theoretical limitation on the sample volume, such that it does not contribute to the shape and width of the elution curve, has been calculated by Glueckauf: [18] the injection band width, w_i, should be less than one-quarter of the emergent band width w_e. This result is equivalent to that suggested later by van Deemter *et al.*,[2] and shown by them to be approximately true in practice. Experiments were carried out in order to ascertain whether this applied in our conditions.

The feed volume was varied by altering the time of injection of the liquid samples. Since the feed width was measured directly, this method is more reliable than that in

[10] Purnell and Quinn, 3rd Symp. Gas Chromatography Discussion Group, Edinburgh, June 1960, Preprints, p. 154; " Gas Chromatography " (ed. Scott), Butterworths, London, 1960, p. 184.
[11] Mellor, as in ref. 6, p. 63.
[12] Pollard and Hardy, as in ref. 6, p. 115.
[13] Littlewood, as in ref. 4, p. 23.
[14] Bohemen and Purnell, *Chem. and Ind.*, 1957, 815; *J. Appl. Chem.*, 1958, **8**, 433.
[15] Ray, *J. Appl. Chem.*, 1954, **4**, 21.
[16] Lichtenfels, Fleck, Burow, and Coggeshall, *Analyt. Chem.*, 1956, **28**, 1376.
[17] Pollard and Hardy, *Chem. and Ind.*, 1955, 1145.
[18] Glueckauf, *Trans. Faraday Soc.*, 1955, **51**, 34.

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which the sampler volume is changed and the feed volume is assumed to be that of the sampler. Both the emergent band width w_e and the feed width w_i were measured directly from the recorder chart with a travelling microscope. Fig. 1 shows a plot of w_e against w_i for the four solutes used; also shown is the line representing the theoretical relation $w_e/w_i = 4$. It is evident that the agreement between theory and experiment is good. Owing to its short retention time, it was never possible to inject cyclohexane rapidly enough to achieve the condition $w_e/w_i > 4$. In fact, when the results contained in Fig. 1 were used to compute the maximum sample of cyclohexane which should be used in the column studies proper it was found that with the solvent and temperature used even the smallest sample which could be handled gave an excessive feed volume. In consequence, the results obtained for this solute are not discussed further. This result emphasises the fact that excessive feed volume is liable to be an important source of the inconsistencies in much published work.

Adsorption by the Support.—Although reduction of the ratio of stationary phase to solid upport may increase the column efficiency,[6,19] increased adsorption of the solute by the

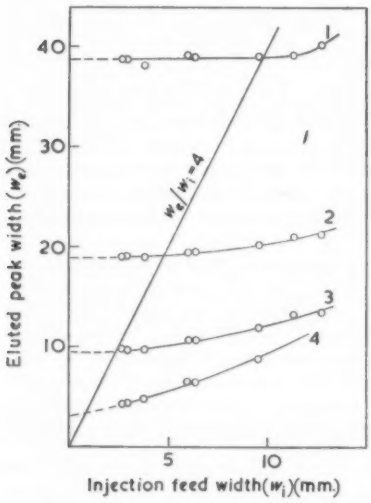

FIG. 1. *Plot of eluted band width against injection band width.*

1, *Propan-2-ol.* 2, *Benzene.* 3, *Acetone.* 4, *Cyclohexane.*

greater uncovered area of the support is likely to cause undesirable band-broadening and -distortion and altered retention volumes.[20] Experiments were carried out to determine the conditions under which the solid support could, for the purposes of this work, be regarded as inert, a condition necessary if evaluation of k' is to be realistic. The specific

TABLE 1. *Variation of specific retention volume with the amount of stationary phase. Column temp.* 51°.

Polyethylene glycol 400 (g.) per 100 g. of Sil-O-Cel		2·0	5·0	10·2	20·1
Spec. retention vol. (V_g) (ml. of N_2):	acetone	103·1	90	87	86
	benzene	195	176	168	165

retention volumes,[21] V_g, of acetone and benzene were determined for different ratios of stationary phase to solid support. These are listed in Table 1, the values quoted being the mean of at least ten measurements over a wide variety of flow rates. They indicate that

[19] Ring, First I.S.A. Symposium, East Lansing, Michigan, August, 1957; Cheshire and Scott, *J. Inst. Petroleum*, 1958, **44**, 74.
[20] Adlard, as in ref. 6, p. 98.
[21] Ambrose, Keulemans, and Purnell, *Analyt. Chem.*, 1958, **30**, 1582.

20% w/w columns of polyethylene glycol on Sil-O-Cel are suitable for use throughout the work subsequently carried out.

The Reproducibility of Column Construction.—Reproducibility was studied by making pairs of columns with supports of different particle sizes. The supports used for the 30—40 mesh columns were prepared from batches of firebrick screened on different occasions, while the 50—60 and 100—150 mesh supports were each screened in one

TABLE 2. *Reproducibility of column construction.*

Mesh range (IMM)	d_p (mm.)	10^2H (cm.) Acetone $\bar{u}$ (cm./sec.) 10	15	Benzene $\bar{u}$ (cm./sec.) 10	15	Mesh range (IMM)	d_p (mm.)	10^2H (cm.) Acetone $\bar{u}$ (cm./sec.) 10	15	Benzene $\bar{u}$ (cm./sec.) 10	15
20—30	0·32	14·1	17·2	16·2	20·2	100—150	0·10	4·7	5·2	4·8	5·3
30—40	0·33	14·4	18·9	15·8	20·3	100—150	0·10	4·6	4·9	4·5	4·9
30—40	0·21	10·3	13·0	11·6	14·6						
50—60	0·16	6·6	6·9	6·6	7·5						
50—60	0·17	6·8	7·5	6·6	7·6						

operation. The efficiencies of these columns were determined many times at each of many different linear gas velocities. From plots of the mean H against the true average linear gas velocity $\bar{u} = u'f/p_0$, the values of H for the different columns at $\bar{u} = 10$ and 15 cm./sec. were evaluated for the comparison illustrated in Table 2.

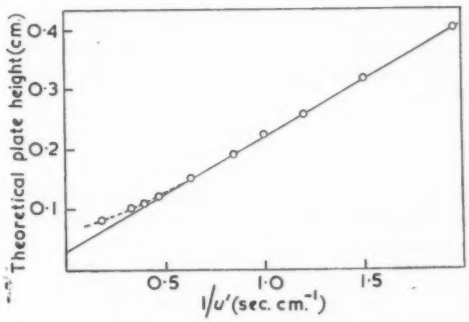

FIG. 2. *Plot of H against 1/u'. Slope = B', intercept = A. Data for elution of benzene by nitrogen at 51° from column of d_p 0·016 cm. Broken line shows increasing importance of C terms at high u'.*

A series of measurements, under fixed conditions, with a given column showed that the reproducibility of H was about $\pm 2{\cdot}5\%$ with the direct injection system. The agreement between the pairs of 50—60 and 100—150 mesh column is thus satisfactory. However, the efficiency of the first 30—40 mesh column listed in Table 2 was much lower than of the other. Permeability measurements showed that the particle size, d_p, of the support in the former was considerably greater than expected, and corresponded reasonably closely to 20—30 mesh (data for a column containing 20—30 mesh Sil-O-Cel are listed for comparison). Thus, our procedure for constructing columns is reasonably reproducible but the findings add weight to the view [1] that d_p can only be evaluated properly for theoretical purposes from studies of column permeability to gas flow.

Coefficient Evaluation.—Up to this time, only a three-constant equation has been employed to represent packed-column data, while several methods of representing the carrier-gas velocity have been used. One common approach is to divide the column length by the air peak-retention time, a procedure which yields $\bar{u}$ for a capillary or glass-bead column but something closer to $\bar{u}/2$ for a column with porous packing.[1] Alternatively, a velocity, u_0, calculated by dividing the rate of gas flow at the column outlet by the free cross-sectional area can be used. For packed columns as well as capillaries the product $u_0 f$ gives the correct value of $\bar{u}$. Evidently, unambiguous determination of u_0, $\bar{u}$, or u' for packed columns requires measurement of free inter-particle cross-sectional area and, hence, of the column bulk-packing density.

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Consideration of equation (1) reveals that, since it contains the three variables H, u' $(= u_0 p_0)$, and $\bar{u}$, there is no two-dimensional graphical method of representing the dependence of H upon velocity from which all coefficients can be simultaneously deduced. If a plot of H against $\bar{u}$ is employed, reasonable values of the C terms may be obtained, but derived values of A and B' will be very much in error. This is no small effect and values of B' which are several times too small can readily be derived for a column of any reasonable length. The methods of evaluating coefficients used in this work were as follows.

A large number of measurements of H, made at low velocities, were plotted as graphs of H against $1/u'$, as in Fig. 2. At very high values of $1/u'$ we can write equation (1) approximately as

$$H = A + B'/u', \tag{4}$$

and so, equally approximately, values of A and B' can be obtained from the intercept and slope of the plot, respectively. There now remains the much more difficult problem of evaluating, even approximately, C_g' and C_l. The method developed for this was based on the use of the following modification of equation (1):

$$H_1 - H_2 = (A_1 - A_2) + \left(\frac{B_1'}{u_1'} - \frac{B_2'}{u_2'}\right) + (C_{g_1}'u_1' - C_{g_2}'u_2') + (C_{l_1}\bar{u}_1 - C_{l_2}\bar{u}_2),$$

the subscripts relating to values obtained for a given solute eluted either in different carrier gases or in the same gas at different outlet pressures.

In principle, both A and C_l are independent of the pressure and identity of carrier gas and so

$$\Delta H = \left(\frac{B_1'}{u_1'} - \frac{B_2'}{u_2'}\right) + (C_{g_1}'u_1' - C_{g_2}'u_2') + C_l(\bar{u}_1 - \bar{u}_2).$$

Because of the difference in the relation of pressure drop to volume flow for different gases or attending overall pressure change for a given gas, it is convenient to eliminate C_l by measuring ΔH at $\bar{u}_1 = \bar{u}_2$ when, of course, $u_1' \neq u_2'$. Then

$$\Delta H = \left(\frac{B_1'}{u_1'} - \frac{B_2'}{u_2'}\right) + (C_{g_1}'u_1' - C_{g_2}'u_2'). \tag{5}$$

The most convenient way to employ this equation was, not to calculate ΔH at different values of u_1' and u_2', but to use plots of H against $\bar{u}$ and to locate the point of crossing of plots, that is, $\Delta H = 0$. That this situation must always arise can be seen from equation (5). If $B_1' > B_2'$, then $C_{g_2}' > C_{g_1}'$, hence, at low velocities the term in the first parentheses contributes predominantly to ΔH and is positive, while at high velocities the second such term predominates and is negative. Thus, at the cross-over point,

$$\frac{B_1'}{u_1'} - \frac{B_2'}{u_2'} = C_{g_2}'u_2' - C_{g_1}'u_1'. \tag{6}$$

Once approximate values of B_1' and B_2' had been obtained, as from Fig. 2, then, since $B_1'/B_2' = C_{g_2}'/C_{g_1}'$, the C_g' terms could be calculated with an accuracy comparable to that of the approximate B' terms. Experience has shown that this is normally better than 25%.

Some evidence was found which indicated that ΔA was not zero with hydrogen as carrier gas. Thus, it was necessary to generalise equation (6) to

$$\Delta A + \left(\frac{B_1'}{u_1'} - \frac{B_2'}{u_2'}\right) = C_{g_2}'u_2' - C_{g_1}'u_1' \tag{7}$$

and to use the approximate value of ΔA found concurrently with B_1' and B_2'.

Whether or not it was necessary to use a value of ΔA, A, B', and C_g' were known and evaluation of C_l for a given system was completed by use of equation (1). All these values were of course approximate, but they served as the basis for subsequent modifications in which the values of the coefficients were altered slightly in turn and the values of calculated

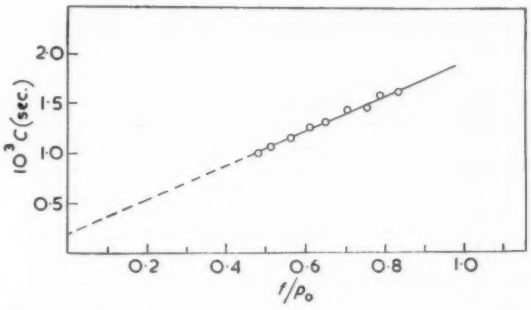

FIG. 3. *Plot, according to equation* (8), *of* C *against* f/p_0. *Data for elution of acetone by nitrogen at* 51° *from column of* d_p 0·010 *cm.*

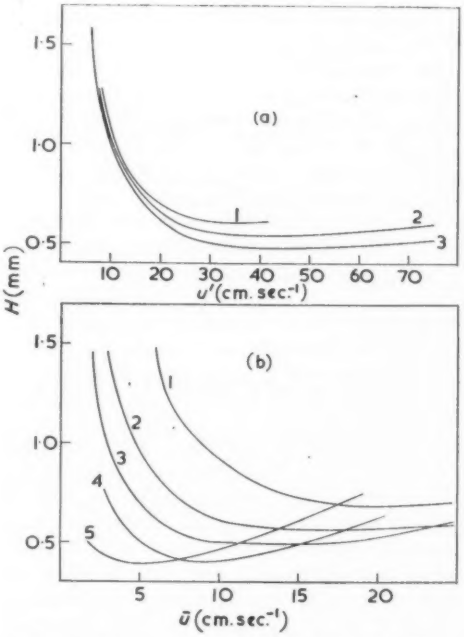

FIG. 4. *Plots of* H *against* (a) u' *and* (b) $\bar{u}$ *for the elution of benzene from column of* d_p 0·010 *cm. at* 51°.

1, Hydrogen, p_0 1 atm. 2, Hydrogen, p_0 2 atm. 3, Hydrogen, p_0 3 atm. 4, Nitrogen, p_0 1 atm. 5, Nitrogen, p_0 3 atm. *Each curve is drawn from at least* 40 *experimental measurements.*

and experimental H compared. This process was continued until the comparison showed an agreement, within the estimated error of measurement of H, over the whole velocity range studied. The procedure is tedious, about six complete operations being usually required, but it has been found to be the most reliable yet devised in the absence of a computor.

A supplementary method of deriving values of C_g' and C_l is based on the following argument. We can write a total mass-transfer coefficient, C, defined by

$$C = fC_l/p_0 + C_g'. \qquad (8)$$

A value of C at any value of H can be calculated for any individual high-velocity datum

with considerable precision, even when the most approximate values of A and B' are used. From equation (8) we see that a plot of C against f/p_0, both of which vary with velocity, should be linear, of slope C_l and intercept C_g'. Fig. 3 shows such a plot, which is seen to fit the relation over a fairly wide range of values of f/p_0. However, there is some uncertainty in the value of C_g' obtained owing to the lengthy extrapolation. Even so, for

TABLE 3. *Rate equation coefficients for acetone and benzene eluted from* 20% w/w *polyethylene glycol* 400/Sil-O-Cel *columns at* 51°.

d_p cm.)	Carrier gas	A (cm.)		B' (cm.^{2} sec.$^{-1}$)		$10^3C_g'$ (sec.)		10^3C_l (sec.)	
		Acetone	Benzene	Acetone	Benzene	Acetone	Benzene	Acetone	Benzene
0·032	H_2	0·040	0·033	0·87	0·78	1·4	1·3	2·4	2·9
	N_2	0·051	0·058	0·210	0·165	5·8	6·2	2·4	2·9
0·016	H_2	0·026	0·011	0·92	0·84	0·3	0·3	1·1	1·6
	N_2	0·034	0·032	0·225	0·190	1·3	1·4	1·1	1,6
0·010	H_2	0·014	0·010	0·96	0·85	0·1	0·1	1·2	1·5
	N_2	0·011	0·009	0·254	0·224	0·4	0·4	1·2	1·5

the plot shown, the value of C_g' obtained was only about 40% lower than that given by the previous method. In order that a sufficiently wide range of f/p_0 values may be

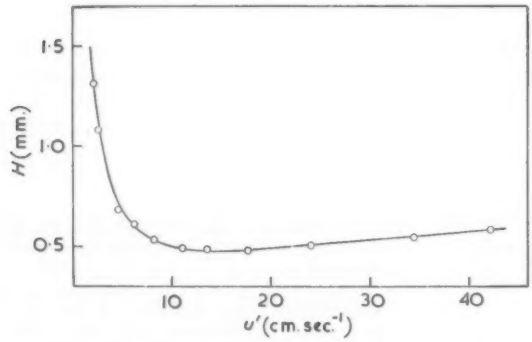

FIG. 5. *Plot of data for acetone eluted by nitrogen at* 51° *from column of* d_p 0·010 *cm.*

Full curve represents equation

$$H = 0{\cdot}011 + 0{\cdot}254/u' + 4 \times 10^{-4}u' + 1{\cdot}2 \times 10^{-3}\,u'f;$$

circles are experimental values.

achieved, say, 1—0·5, it is necessary to use a column at least 5 ft. long if the support is of 100—150 mesh, or 30 ft. if it is of 30—40 mesh.

Evaluated Data for Acetone and Benzene.—Coefficients were evaluated for acetone and benzene eluted from columns with supports of different sizes in experiments with hydrogen and nitrogen at outlet column pressures of 1—3 atm. at 51°; they are listed in Table 3. An example of the type of H–$\bar{u}$ plots obtained, with the corresponding H–u' plots, is shown in Fig. 4. The former (b) show the crossings predicted by equation (5), while the latter (a) substantiate the pressure corrections introduced into equation (1) since the curves tend to coincide at low velocity and move apart at high velocity. The results in Table 3 reproduce the experimental values of H to about ±1% over the velocity range 1—70 cm. sec.$^{-1}$, an example of the fit being shown in Fig. 5. Table 4 lists results deduced from those contained in Table 3 which are helpful in the further discussion. The values of λ quoted for nitrogen and hydrogen elution of both acetone and benzene are all very close to unity. On the other hand, those for hydrogen elution are not only most often lower than for nitrogen elution, but are also lower for benzene than for acetone. This peculiarity associated with hydrogen has been noted previously.[1,22] It seems a safe conclusion that, for the columns used here, λ is not greater than unity, the mean value being 0·86. A mean value of $\lambda = 0{\cdot}83$ was found [1] for the elution in nitrogen of both hydrogen and carbon dioxide from the same three columns. These results cannot be

[22] Glueckauf, as in ref. 4, p. 33.

taken to imply that eddy diffusion as originally envisaged [2] operates in these systems, since the variations observed may, for example, reflect channelling effects. It is noticeable, for instance, that when $\lambda_{N_2}/\lambda_{H_2}$ is greater than unity for either benzene or acetone, $\gamma_{N_2}/\gamma_{H_2}$ is less than unity, and *vice versa*.

TABLE 4. *Rate equation terms evaluated from data in Table* 3. *Recorded values of* D_g' *used*: *acetone* $(N_2) = 0{\cdot}120$; *benzene* $(N_2) = 0{\cdot}105$; *acetone* $(H_2) = 0{\cdot}467$; *benzene* $(H_2) = 0{\cdot}411$ *cm.*^{2} *sec.*$^{-1}$.

d_p	λ		γ			χ		
(cm.)	N_2	H_2	N_2	H_2	B_{H_2}'/B_{N_2}'	N_2	H_2	$10^3 d_f^2/D_l$
Acetone					(theor. = 3·9)			
0·032	0·8	0·62	0·87	0·93	4·15	1·7	1·6	4·4
0·016	1·1	0·8	0·94	0·99	4·1	1·5	1·4	2·1
0·010	1·1	1·4	1·06	1·03	3·8	1·3	1·2	2·4
Benzene					(theor. = 3·9)			
0·032	0·9	0·52	0·79	0·95	4·7	1·5	1·3	9·4
0·016	1·0	0·34	0·91	1·02	4·4	1·3	1·1	5·5
0·010	0·9	1·0	1·07	1·03	3·8	1·3	1·0	5·5

An alternative explanation is that errors in the estimations of λ and γ are sufficient to cloud the issue. The ratios B_{H_2}'/B_{N_2}', while remarkably close to the theoretical value, when all is considered, show fairly large and random variations from system to system which are, in turn, reflected in γ and also in the variation of $\lambda_{N_2}/\lambda_{H_2}$. It is thus possible that λ merely represents the cumulative error involved in the elucidation of the other coefficients and that, in fact, $\lambda = 0$, as was postulated at one time by the authors.[7]

With one exception, all the values of γ quoted in Table 4 lie above 0·87. The probable error in the results is estimated at not less than $\pm 0{\cdot}06$. This estimate must be realistic since it is clear from the Table that values greater than unity, which are theoretically inadmissible, can be found. Since the mean of the results is 0·96, in the light of the immediately previous discussion it appears likely that, as in the elution of unsorbed gases, γ is unity.[1]

Considerable confidence in the essential correctness of equation (1) and the approach to the evaluation of the coefficients is derived from the quoted values of χ, which were calculated by comparison of the experimentally measured C_g' with equation (2). These range from 1·1 to 1·7, while for a given column no significant difference is observed between the values for hydrogen and nitrogen elution or between the data for acetone and benzene. Further, little change in χ is observed from d_p 0·032 to 0·016 cm. while C_l is halved. There appears to be a trend towards lower values of χ at low d_p but, again, computational errors are sufficient to make this too uncertain to merit discussion at this time. No great error is introduced if the mean value $\chi = 1{\cdot}5$ is taken as a general figure.

The data for the function d_f^2/D_l were calculated from C_l and k' values by using equation (3). These show that halving the particle size from 0·032 to 0·016 cm. almost exactly halves the function. Since D_l is presumably constant this implies that in this range of particle size $d_f \propto d_p^{\frac{1}{2}}$. On the other hand, on going from d_p 0·016 to 0·010 cm., d_f^2/D_l is virtually unchanged for both solutes. These variations might be attributed to error, were it not for the essential constancy of χ already noted and the accuracy with which C can be measured. The results, therefore, imply that solvent distribution is mainly of the droplet, and not of the film, type, the droplet size being determined by the identity, temperature, and pore structure of the solid support rather than by the particle size of the latter. Only with the coarsest support is the film thickness a function of particle size. If it is assumed that D_l for acetone is 10^{-7} cm.^{2} sec.$^{-1}$ the value of d_f for the two finer-mesh columns is $1{\cdot}6 \times 10^{-3}$ cm. This result is reasonable and corresponds well with general opinion. Since d_f is constant the results show that the ratio of D_l for benzene and acetone is 2·2 when $d_p = 0{\cdot}032$ cm., and 2·3 when $d_p = 0{\cdot}010$ cm. This remarkable

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constancy again supports the view that the derived values of d_f^2/D_l are realistic and that the function is important and occurs as written in the van Deemter equation.

The conclusions to be drawn from this and the earlier work [1] are that the rate equation for packed columns of porous support, such as were used in this work, can be written:

$$H = 1{\cdot}5d_p + \frac{2D_g'}{u'} + \frac{[1 + 6k' + 11(k')^2]d_p^2u'}{16(1 + k')^2D_g'} + \frac{2}{3}\frac{k'}{(1 + k')^2}\frac{d_f^2\bar{u}}{D_l}, \quad (9)$$

the need to include the term $1{\cdot}5d_p$ being, perhaps, particular to the systems used here.

With the exception of the function d_f^2/D_l, every quantity in this equation can be measured by other than chromatographic methods. It seems, therefore, that further experiments designed to check the present findings, as expressed in equation (9), and to provide means of independent evaluation of d_f and D_l would be worth while. If the latter is achieved and equation (9) is further supported it should be possible to eliminate much of the effort now expended in column characterisation, in particular that carried out with analysis of maximum speed in view.

In connection with the latter, the finding that, with nitrogen as carrier gas, $C_g' \approx 2{\cdot}5C_l$ for the column of coarsest support, while $3C_g' \approx C_l$ for that with the finest support, is of considerable importance. It means that the conditions for fastest analysis are very different in the two cases,[10] and so the theory of high-speed analysis with packed columns must be extended to take this into account. Since, also, C_g' is so much greater in nitrogen than in hydrogen, it is evident that for fastest analysis the latter is the more desirable carrier. Finally, since it is clear that fastest analysis demands the smallest d_p, when, even in nitrogen, C_l is predominant, the key to higher speed lies in finding means of reducing resistance to mass transfer in solution.

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Department of Physical Chemistry, The University,
Lensfield Road, Cambridge.
[Present address (J. B.): Chemistry Department, Princeton University,
Princeton, New Jersey.] [*Received, November 1st*, 1960.]

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516. *Triterpenoids. Part LVIII.* The Synthesis of Isoursenol, the Ursane Analogue of Taraxerol.*

By William Laird, F. S. Spring, and Robert Stevenson.

The conversion of α-amyrin (VI; R = H) into isoursenol (X; R = H) is described; the behaviours of taraxerol and isoursenol on oxidation by peracid are compared.

Most of the naturally occurring pentacyclic triterpenoids can be classified in the oleanane, ursane, and lupane groups although it is now appreciated that this division is biogenetically without significance, all three groups being unexceptionally derivable from the prelupeol cation (I).[1] Further, simple derivatives of ursane and lupane have been converted into oleanane derivatives. Although the naturally occurring ketones, taraxerone [2] (II), glutinone [3] (alnusenone) (III), and friedelin [4] (IV) do not have an oleanane

* Part LVII, *J.*, 1959, 216.

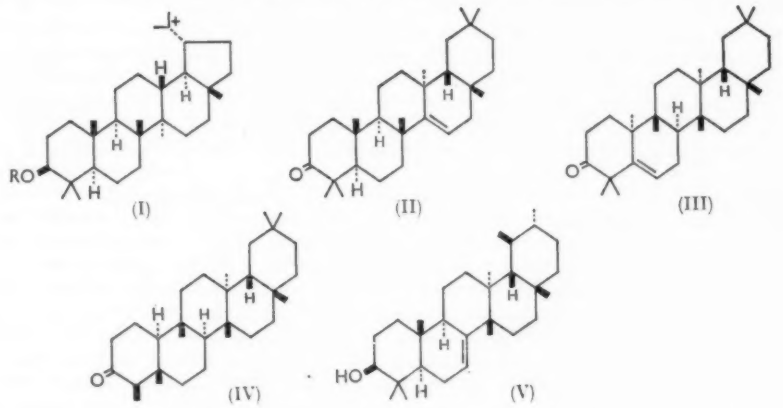
[1] Ruzicka, *Experientia*, 1953, **9**, 357; Eschenmoser, Ruzicka, Jeger, and Arigoni, *Helv. Chim. Acta*, 1955, **38**, 1890; Ruzicka, "Perspectives in Organic Chemistry," ed. Todd, Interscience Publ. Inc., New York, 1956.

[2] Beaton, Spring, Stevenson, and Stewart, *J.*, 1955, 2131.

[3] Beaton, Spring, Stevenson, and Stewart, *Tetrahedron*, 1958, **2**, 246.

[4] Brownlie, Spring, Stevenson, and Strachan, *J.*, 1956, 2419; Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041; Takahashi and Ourisson, *Bull. Soc. chim. France*, 1956, 353.

skeleton, they have been converted by acid-isomerisation of derived ethylenic hydrocarbons into a mixture of olean-13(18)-ene and 18α-olean-12-ene. They can consequently be regarded as members of a new sub-group, the " modified oleanane " group, which can be defined as consisting of pentacyclic triterpenes which by acid-isomerisation of suitable derivatives yield an oleanane derivative by migration of angular methyl groups or hydrogen atoms by a series of formal 1,2-shifts from and to axial conformations.



The existence of the modified oleanane group has been readily rationalized in current theories of biogenesis. On biogenetic grounds, the existence of a " modified ursane " group would also be considered extremely probable, although no ursane analogues of taraxerone, glutinone, or friedelin have been described. The report by Lahey and Leeding [5] of the isolation and structure of bauerenol (ilexol) (V) establishes it as the first naturally occurring member of the " modified ursane " class. The partial synthesis from α-amyrin (VI; R = H) of isoursenol (X; R = H), the ursane analogue of taraxerol and second member of the modified ursane group, is now reported.

The synthetic route corresponded to that developed for the partial synthesis of taraxerol from β-amyrin.[2] The conversion of 12-oxours-9(11)-en-3β-yl acetate (VII) into 12-oxoisoursa-9(11),14-dien-3β-yl acetate (VIII) by selenium dioxide [6] was improved by curtailing the reaction time. The subsequent reduction by lithium in liquid ammonia and ether to give 12-oxoisours-14-en-3β-ol (IX) [7] was similarly improved. Application of the Barton modification of Huang-Minlon reduction to this alcohol, followed by acetylation, gave isoursenyl acetate (X; R = Ac) in over 50% yield; the alcohol (X; R = H) and benzoate (X; R = Bz) were prepared in the usual way. Under certain conditions of the forcing reduction, the intermediate 12-oxoisours-14-en-3β-yl acetate hydrazone was also isolated; it was characterized as the acetylhydrazone.

The physical constants of isoursenol and its derivatives are similar to those of calendenol, $C_{30}H_{50}O$, and its derivatives, isolated by Kasprzyk,[8] but direct comparison with a sample provided by Dr. Kaspryzk established the dissimilarity of these substances.

The behaviour of taraxeryl acetate towards mineral acid—molecular rearrangement to β-amyrin acetate—is paralleled by the clean conversion of isoursenyl acetate (X; R = Ac) into α-amyrin acetate (VI; R = Ac) under the same conditions.

Treatment of isoursenyl acetate with perbenzoic acid yielded two isomeric products,

[5] Lahey and Leeding, *Proc. Chem. Soc.*, 1958, 342.
[6] Ruzicka, Rüegg, Volli, and Jeger, *Helv. Chim. Acta*, 1947, **30**, 140; Easton and Spring, *J.*, 1955, 2120.
[7] Beaton, Easton, Macarthur, Spring, and Stevenson, *J.*, 1955, 3992.
[8] Kasprzyk, *Prace Glöwnego Inst. Chem. Przemysl*, 1951, No. 2, 39; *Chem. Abs.*, 1953, **47**, 6918.

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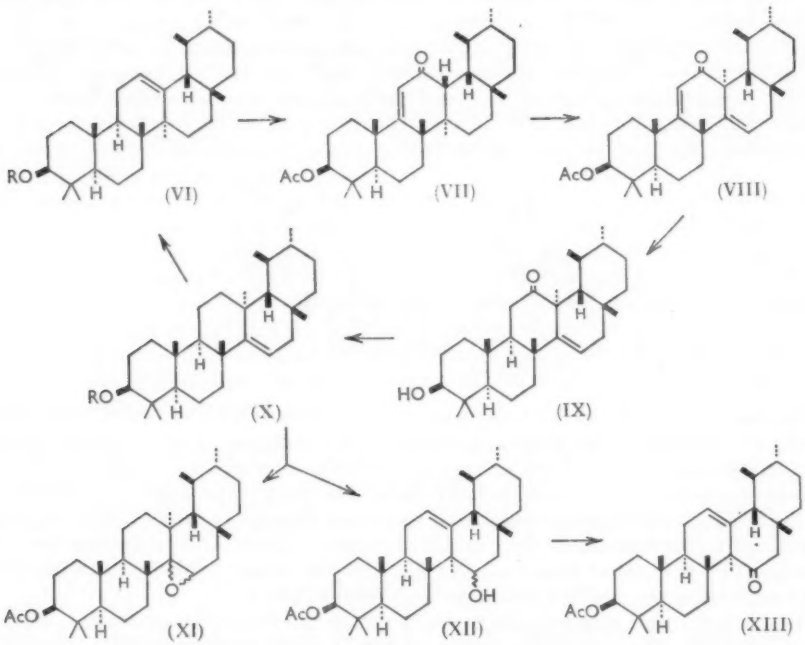
$C_{32}H_{52}O_3$, readily separated by chromatography on alumina. The more readily eluted product shows no high-intensity ultraviolet absorption, does not give a colour with tetranitromethane, and is considered to be isoursenyl acetate oxide (XI). The second product, however, possesses a double bond (yellow colour with tetranitromethane, ultraviolet absorption) and a hydroxyl group. In analogy with the behaviour of taraxeryl acetate for which the structures of the peracid oxidation products were rigorously established, the second product is tentatively considered to be 3β-acetoxyurs-12-en-15ξ-ol (XII). This



diol monoacetate is also readily obtained by the action of mineral acid on the oxide (XI) in chloroform–methanol or acetic acid, and with the chromium trioxide–pyridine reagent gave a non-conjugated ketone formulated here as 15-oxours-12-en-3β-yl acetate (XIII).

Although in this behaviour towards perbenzoic acid isoursenyl acetate resembles taraxeryl acetate, structures of the products cannot be assigned with certainty, for the following reasons. The diol monoacetate, formulated as (XII), resists acetylation under conditions whereby 3β-acetoxyolean-12-en-15α-ol is acetylated. Further, the rotatory disperion curve of the derived ketone, formulated as (XIII), shows a positive Cotton effect in contrast to the negative Cotton effect shown by the oleanan-15-one derivative, 15-oxoerythrodiol diacetate.[9] Although these differences between the two series are possibly explicable by conformational distortion in the C/D/E region of the ursane series, as compared with the oleanane series, the possibility that the molecular rearrangement undergone by the isoursenyl acetate oxide on treatment with mineral acid is not of isoursenol ⟶ α-amyrin type has not been excluded.

Experimental

Rotations were measured for $CHCl_3$ and ultraviolet absorption spectra for EtOH solutions. Grade II alumina and light petroleum of b. p. 60—80° were used for chromatography.

[9] Djerassi, Osiecki, and Closson, *J. Amer. Chem. Soc.*, 1959, **81**, 4587.

12-*Oxoisoursa*-9(11),14-*dien*-3β-*yl Acetate* (VIII).—A solution of 12-oxours-9(11)-en-3β-yl acetate (36 g.) in glacial acetic acid (580 c.c.) was refluxed for 2 hr. with selenium dioxide (54 g.). The product, isolated in the usual way, crystallized from methanol to give needles (23 g.), m. p. 220—221°, $[\alpha]_D$ +14·5° (*c* 6·1), a solution of which in benzene–light petroleum (1 : 4; 1 l.) was chromatographed on alumina (1 kg.). Elution with light petroleum–benzene (3 : 2, 4 l.; 1 : 1, 2·5 l.; 2 : 3, 3·5 l.) yielded 12-oxoisoursa-9(11),14-dien-3β-yl acetate (17·5 g.) as needles (from methanol), m. p. 218—220°, $[\alpha]_D$ +8·5° (*c* 3·3), $\lambda_{max.}$ 2370 Å (ε 10·000) (lit.,[6] m. p. 221—222°, $[\alpha]_D$ +8°).

12-*Oxoisours*-14-*en*-3β-*ol* (IX).—A solution of 12-oxoisoursa-9(11),14-dien-3β-yl acetate (2·0 g.) in dry ether (100 c.c.) was added in 2 min. with stirring to a solution obtained by adding lithium (600 mg.) to liquid ammonia (400 c.c.), and the mixture was stirred for a further 3 min. After the addition of acetone, the product was isolated in the usual manner and crystallized from methanol, to give 12-oxoisours-14-en-3β-ol (0·8 g.) as needles, m. p. 230—231°, $[\alpha]_D$ −39° (*c* 1·4) (lit.,[7] m. p. 233—234°, $[\alpha]_D$ −39°), ε 5500 at 2050 Å, giving a yellow colour with tetranitromethane.

Isours*-14-*en*-3β-*yl Acetate (X; R = Ac).—12-Oxoisours-14-en-3β-ol (1·0 g.) was added to a solution obtained by the addition of sodium (2·5 g.) to freshly distilled diethylene glycol (125 c.c.) and the mixture heated to 180°. Anhydrous hydrazine was distilled into the mixture until the solution refluxed gently at 180°. After refluxing at this temperature for 18 hr., the mixture was distilled until the temperature rose to 210°, whereafter refluxing was continued for 24 hr. The product, isolated by means of ether, was treated on the steam-bath with acetic anhydride and pyridine. The product was dissolved in light petroleum, filtered through alumina (40 g.), and crystallized from methanol to give *isours*-14-*en*-3β-*yl acetate* (250 mg.) as plates, m. p. 214—216°, $[\alpha]_D$ +36° (*c* 1·3) (Found: C, 81·9; H, 11·4. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). It gives a yellow colour with tetranitromethane.

Elution with light petroleum–benzene (9 : 1; 200 c.c.) gave 12-oxoisours-14-en-3β-yl acetate (300 mg.), m. p. and mixed m. p. 227—228°, $[\alpha]_D$ −27° (*c* 0·8).

The residue obtained on elution with methanol–benzene crystallized from methanol, to give 12-*oxoisours*-14-*en*-3β-*yl acetate hydrazone* as needles (350 mg.), m. p. 245—247°, $[\alpha]_D$ +19° (*c* 1·2), $\lambda_{max.}$ 2120 and 2370 Å (ε 12,400 and 10,000), ν (in CS_2) 3175, 1736, and 1675 cm.$^{-1}$ (Found: C, 76·9, 77·3; H, 10·4, 10·1; N, 5·2. $C_{32}H_{52}N_2O_2$ requires C, 77·4; H, 10·55; N, 5·6%). It gives a yellow colour with tetranitromethane. Refluxing the hydrazone with acetic anhydride for 2 hr. gave the *acetylhydrazone* as prisms, m. p. 201—202°, $[\alpha]_D$ +35° (*c* 1·4), $\lambda_{max.}$ 2040 and 2390 Å (ε 8400 and 5000), ν (in CS_2) 1736, 1718, and 1667 cm.$^{-1}$ (Found: C, 75·6; H, 10·1; N, 5·0. $C_{34}H_{54}N_2O_3$ requires C, 75·8; H, 10·1; N, 5·2%).

Isoursenyl acetate was isolated in 55% yield without contamination by hydrazone if the entire reduction process was repeated with fresh hydrazine.

Isours*-14-*en*-3β-*ol (X; R = H).—A solution of isoursenyl acetate (250 mg.) in ether (150 c.c.) was refluxed with lithium aluminium hydride (250 mg.), and the product, isolated in the usual way, crystallized from methanol to give *isours*-14-*en*-3β-*ol* as needles, m. p. 195—197°, $[\alpha]_D$ +30° (*c* 1·6) (Found: C, 84·1; H, 11·6. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). Reacetylation gave isoursenyl acetate, m. p. and mixed m. p. 214—216°, $[\alpha]_D$ +35° (*c* 1·1). Benzoylation yielded *isours*-14-*en*-3β-*yl benzoate*, as blades (from chloroform–methanol), m. p. 237—239°, $[\alpha]_D$ +55° (*c* 2·0) (Found: C, 83·3; H, 10·3. $C_{37}H_{54}O_2$ requires C, 83·7; H, 10·25%).

Conversion of Isoursenyl Acetate into α-Amyrin Acetate.—To a suspension of isoursenyl acetate (25 mg.) in acetic acid (15 c.c.) at 100° was added concentrated hydrochloric acid (2 c.c.). After the mixture had been heated for 25 min., the solvent was removed under reduced pressure. The residue crystallized from methanol to give α-amyrin acetate (urs-12-en-3β-yl acetate), plates, m. p. and mixed m. p. 221—223°, $[\alpha]_D$ +77° (*c* 0·7).

Action of Perbenzoic Acid on Isoursenyl Acetate.—A solution of isoursenyl acetate (750 mg.) in chloroform (10 c.c.) was treated with a fresh solution of perbenzoic acid (2·0 mol.) in chloroform and set aside at 0° for 18 hr., then washed with sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated below 15°. The residue was chromatographed in light petroleum–benzene (9 : 1; 100 c.c.). Elution with light petroleum–benzene (4 : 1; 300 c.c.) gave a solid which recrystallized from chloroform–methanol to give 14ξ,15ξ-*epoxyisoursan*-3β-*yl acetate* (XI) (320 mg.), plates, m. p. 249—251°, $[\alpha]_D$ +57° (*c* 1·0) (Found: C, 79·5; H, 10·8. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). It gives no colour with tetranitromethane and shows no high-intensity ultraviolet absorption above 2000 Å. Elution with benzene (300 c.c.) yielded a

solid which crystallized from aqueous methanol to give 3β-*acetoxyurs*-12-*en*-15ξ-*ol* (XII), needles, m. p. 223—225°, $[\alpha]_D$ +75° (*c* 1·5) (Found: C, 79·0; H, 11·1. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). It gives a yellow colour with tetranitromethane. It was recovered unchanged on attempted acetylation at room or steam-bath temperature.

Acid Rearrangement of 14ξ,15ξ-*Epoxyisoursan*-3β-*yl Acetate*.—(*a*) 2N-Sulphuric acid (5 c.c.) was added to a solution of the epoxide (100 mg.) in acetic acid (100 c.c.), and the mixture heated on the steam-bath for 30 min. The product, isolated in the usual way, was chromatographed in light petroleum (10 c.c.) on alumina, and the fraction eluted by benzene–ether (9 : 1; 300 c.c.) crystallized from aqueous methanol to give 3β-acetoxyurs-12-en-15ξ-ol (45 mg.), m. p. and mixed m. p. 222—225°, $[\alpha]_D$ +73° (*c* 0·8). (*b*) Concentrated hydrochloric acid (4 c.c.) and water (4 c.c.) were added to a solution of the epoxide (200 mg.) in methanol (100 c.c.) and chloroform (30 c.c.). The mixture was set aside at room temperature for 18 hr., and the product isolated in the usual manner and crystallized from aqueous methanol to give the diol monoacetate (125 mg.), m. p. and mixed m. p. 222—225°, $[\alpha]_D$ +75° (*c* 1·1).

15-*Oxours*-12-*en*-3β-*yl Acetate* (XIII).—A solution of 3β-acetoxyurs-12-en-15ξ-ol (275 mg.) in pyridine (10 c.c.) was added to a solution of chromium trioxide (1·0 g.) in pyridine (10 c.c.) and set aside for 16 hr. The product was isolated by means of ether and crystallized from aqueous methanol to give 15-*oxours*-12-*en*-3β-*yl acetate* (195 mg.), needles, m. p. 220—222° $[\alpha]_D$ +128°, +129° (*c* 0·8, 0·85) (Found: C, 79·4; H, 10·4. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%). It gives a yellow colour with tetranitromethane. Rotatory dispersion in dioxan (*c* 0·050) (kindly determined by Professor C. Djerassi): $[\alpha]_{700}$ +43°; $[\alpha]_{589}$ +62°; $[\alpha]_{321}$ +450°; $[\alpha]_{275}$ −700°.

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517. *Steric Effects in Di- and Tri-arylmethanes. Part VI.* Nucleophilic Replacements in Triphenylmethane Dyes.*

By C. C. BARKER and G. HALLAS.

Steric hindrance of the central carbon atom in basic triphenylmethane dyes facilitates replacement of a terminal dimethylamino-group by a hydroxy-group with formation of a fuchsone, Sufficient hindrance also permits replacement of a dimethylamino-group in the dye base.

THE possibility of achieving nucleophilic replacements in triarylcarbonium ions is demonstrated by the formation of *pp'*-dibromo-*p''*-chlorotriphenylmethyl bromide from *pp'p''*-tribromotriphenylmethyl chloride in liquid sulphur dioxide,[1] but examples are rare. Nucleophilic replacements are, however, quite common in basic triphenylmethane dyes, one of the earliest examples being the formation [2] of Diphenylamine Blue base (I; R = Ph) by heating Pararosaniline base (I; R = H) with aniline in the presence of a little benzoic acid which presumably acts by forming the reactive Pararosaniline ion. Other *para*-groups that readily undergo replacement are the ethoxy-, chloro-, and sulpho-group,[2] and it is now shown that the *p*-dimethylamino-group can be replaced by the hydroxy-group.

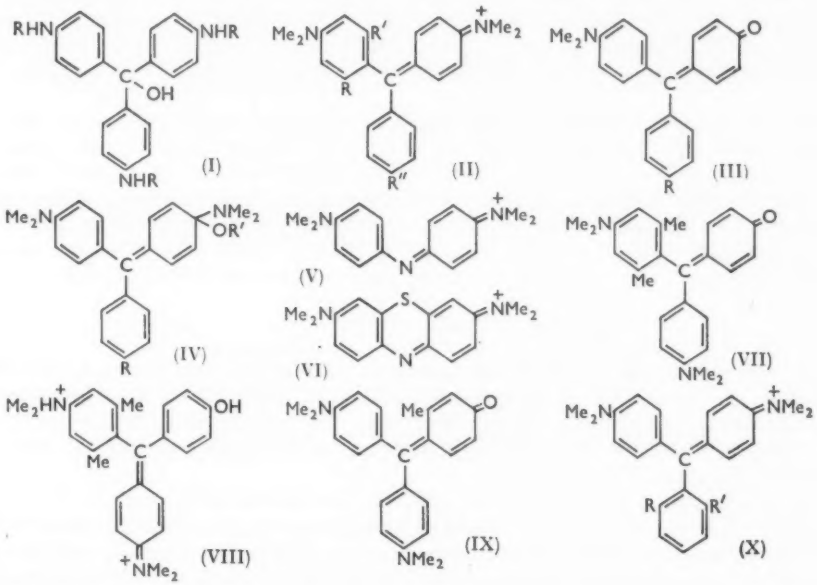
Addition of dilute, aqueous sodium hydroxide to Crystal Violet (II; R = R' = H,

* Part V, *J.*, 1961, 1529.

[1] Gomberg, *Ber.*, 1909, **42**, 406.

[2] Thorpe, "Dictionary of Applied Chemistry," Longmans, Green and Co., London, 1954, Vol. II, p. 689.

R″ = NMe_2), Malachite Green (II; all R's = H), or such of their derivatives as are not highly hindered at the central carbon atom, yields the dye base contaminated by reddish-brown impurities which are probably fuchsone derivatives of type (III; R = NMe_2 or H). These dye bases are stable to alkali and the fuchsones are assumed to arise through a competing reaction between the dye ion and the hydroxide ion, leading to an intermediate (IV; R = NMe_2 or H, R′ = H) which subsequently eliminates dimethylamine. This formulation of the reaction is consistent with the complete absence of red impurities



in the methyl ethers of the dye bases prepared by treating these dyes with methanolic sodium methoxide; the intermediate (IV; R = NMe_2 or H, R′ = Me) would not eliminate trimethylamine and thus form the fuchsone. This smooth preparation of pure methyl ethers has been utilised to obtain spectroscopically pure dyes.[3] Addition of a strong solution of sodium hydroxide to Crystal Violet gives considerable amounts of a reddish-brown material [4] which is probably a secondary product formed by the action of strong alkali on the 4′,4″-bisdimethylaminofuchsone (III; R = NMe_2) first formed; the last compound can be obtained by the basification of the 4-hydroxy-derivative of Malachite Green [5] and it undergoes change readily.

Replacement of the dimethylamino-group becomes predominant whenever dye-base formation is prevented or made difficult. Thus Bindschedler's Green (V) and Methylene Blue (VI), in which the presence of a central nitrogen atom instead of a central carbon atom prevents the formation of non-ionised base, readily lose dimethylamine with alkali,[6] and the highly hindered 2,6-dimethyl derivative of Crystal Violet (II; R = R′ = Me, R″ = NMe_2) gives 4′,4″-bisdimethylamino-2′,6′-dimethylfuchsone (VII) quantitatively after several hours, whereas with methanolic sodium methoxide the dye is unchanged after 14 days. The structure of this fuchsone is established by its absorption spectra in different solvents. In non-acidic solvents the single band in the visible region shows a

[3] Barker, Bride, Hallas, and Stamp, *J.*, 1961, 1285.
[4] Freundlich and Loser, *Z. phys. Chem.*, 1906, **59**, 303.
[5] Ghosh and Watson, *J.*, 1917, 826.
[6] Möhlau, *Ber.*, 1883, **16**, 2855; Bernthsen, *Ber.*, 1906, **39**, 1808.

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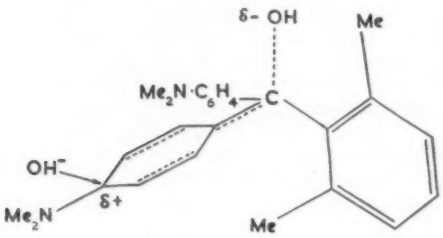
bathochromic shift when a solvent of higher dielectric constant is used [*e.g.*, $\lambda_{max.}$ (in C_6H_6) 477 mμ, ε 31,400; $\lambda_{max.}$ (in MeOH) 562 mμ, ε 51,000], an effect which is consistent with the aminofuchsone structure. In 98% acetic acid two bands are shown in the visible region. The first of these ($\lambda_{max.}$ 635 mμ; ε 28,300) is the first band of the univalent ion (II; R = R′ = Me, R″ = OH), whereas the second ($\lambda_{max.}$ 500 mμ; ε 33,300) is probably the second band of the same ion superimposed on the first band of the bivalent ion (VIII). The latter ion ($\lambda_{max.}$ 507 mμ; ε 38,000) is formed completely when the acidity of the acetic acid is increased by addition of water or hydrochloric acid, and this ready formation of the bivalent ion, coupled with the low intensity of the first band of the univalent ion, shows that the *o*-methyl groups are not situated on the quinonoid nucleus. 4′,4″-Bisdimethylamino-2-methylfuchsone (IX) in acetic acid gives a normal Malachite Green spectrum.[3]



(Reproduced, with permission, from "Steric Effects in Conjugated Systems," Ed. Gray, Butterworths, London, 1959, p. 42.)

The stability of the dimethylamino-group on the xylyl nucleus in the 2,6-dimethyl derivative of Crystal Violet is consistent with the view [7] that it is the xylyl group rather than the phenyl group which relieves steric strain by twisting about the central bond. The terminal nitrogen atom of the xylyl group is thus partially deconjugated from the central carbon atom.

The 2,6-dimethyl-, 2-t-butyl-, and 2-iodo-derivative of Malachite Green (X; R = R′ = Me; R = H, R′ = Bu^t; and R = H, R′ = I, respectively) with sodium hydroxide also give the corresponding fuchsones by replacement of a dimethylamino-group, and from the first of these dyes dimethylamine was isolated as the picrate, m. p. and mixed m. p. 158—160°. These fuchsones were not obtained pure but their red solutions again showed a bathochromic shift on changing from solvent benzene to solvent methanol.

With alkali under vigorous conditions, highly hindered dye *bases* can lose a dimethylamino-group. Thus, the 2,6-dimethyl and 2-t-butyl derivative of Malachite Green base, obtained from Michler's ketone and the appropriate aryl-lithium compound,[3] are converted into the corresponding fuchsones when boiled with aqueous-ethanolic sodium hydroxide, whereas Malachite Green base and its 2-methyl derivative are stable under these conditions. In the more highly hindered dye bases, nucleophilic replacement of a dimethylamino-group is sterically assisted by the reduction of strain which occurs on removal of the central hydroxy-group (see Figure).

Experimental

4′,4″-Bisdimethylamino-2′,6′-dimethylfuchsone.—A 1% aqueous solution of the 2,6-dimethyl derivative of Crystal Violet (chloride [7]) containing 3 equivalents of sodium hydroxide was kept for 48 hr. The red precipitate was dried and crystallised from benzene, giving the *fushsone*, m. p. 214° (Found: C, 80·5; H, 7·6; N, 7·7. $C_{25}H_{28}N_2O$ requires C, 80·6; H, 7·5; N, 7·5%).

One of us (G. H.) thanks the Department of Scientific and Industrial Research for a grant.

The University, Hull. [*Received, November 7th,* 1960.]

[7] Barker, Bride, and Stamp, *J.*, 1959, 3957.

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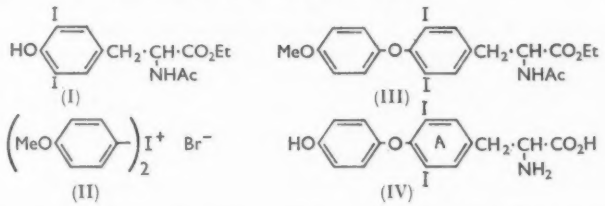
518. *The Synthesis of Thyroxine and Related Compounds. Part XV.*[1] *The Preparation of Thyronines from Iodonium Salts and Derivatives of 3,5-Disubstituted Tyrosines.*

By A. Dibbo, L. Stephenson, T. Walker, and W. K. Warburton.

Hillmann's method [2] for preparing 3,5-di-iodo-L-thyronine has been extended to other 3,5-disubstituted thyronines and to a 4-*p*-hydroxyphenoxyacetic acid. The reaction is improved by using soluble di-*p*-methoxyphenyliodonium salts and methods for preparing these are described. The reaction is also suitable for preparing thyronines containing two different halogens in ring A, one of which may be fluorine.

Interest in the biochemical behaviour of 3,5-dihalogenothyronines has led us to examine the scope of Hillmann's method [2] for preparing 3,5-di-iodo-L-thyronine. Hillmann [2b] refluxed *N*-acetyl-3,5-di-iodo-L-tyrosine ethyl ester (I) for 80 hr. with two equivalents of the sparingly souble di-*p*-methoxyphenyliodonium bromide (II) in methanol containing one equivalent of magnesium methoxide; he isolated *N*-acetyl-3,5-di-iodo-4-*p*-methoxyphenoxy-L-phenylalanine ether ester (III) which, when decomposed with hydrobromic acid, gave 3,5-di-iodo-L-thyronine (IV) in 40% overall yield.



Iodonium halides decompose on prolonged heating.[3] We therefore studied the preparation of alcohol-soluble di-*p*-methoxyphenyliodonium salts, which we expected to react more quickly than the bromide. Treating the bromide [4] or iodide [5] with silver sulphate gave the soluble iodonium sulphate almost quantitatively, and from this we obtained the chloride, which is more soluble than the bromide. The soluble trifluoroacetate was prepared by known methods,[6,7] which, slightly modified,[8] gave di-*p*-methoxyphenyliodonium trichloroacetate in 58% yield at less cost.

Di-*p*-methoxyphenyliodonium trichloroacetate is soluble in boiling methanol, in which it quickly decomposes. It is unsuitable for use in the condensation, but when heated in benzene it rapidly decomposes, giving almost pure di-*p*-methoxyphenyliodonium chloride in 92% yield. This provides a convenient route to a compound ideal for use in the condensation. Although we have not investigated the mechanism of the decomposition, we think it very probable that the trichloroacetate ion undergoes decarboxylation and the intermediate CCl_3^- ion decomposes into chloride ion and dichlorocarbene. It has been shown [9] that the decomposition of sodium trichloroacetate in non-protonic solvents and in the presence of a dichlorocarbene acceptor follows this course. We were not able to

[1] Part XIV, *J.*, 1960, 2711.
[2] Hillmann, (*a*) *Z. Naturforsch.*, 1956, **11**b, 419; (*b*) U.S.P. 2,886,592.
[3] Beringer and Mausner, *J. Amer. Chem. Soc.*, 1950, **80**, 4535.
[4] Plati, U.S.P. 2,839,583.
[5] Mastropaolo, *Anales Asoc. quím. argentina*, 1940, **28**, 101; Beringer, Brierley, Drexler, Gindler, and Lumpkin, *J. Amer. Chem. Soc.*, 1953, **75**, 2708.
[6] Beringer, Bachofer, Falk, and Leff, *J. Amer. Chem. Soc.*, 1958, **80**, 4279.
[7] Beringer, Falk, Karniol, Lillian, Masulo, Mausner, and Sommer, *J. Amer. Chem. Soc.*, 1959, **81**, 342.
[8] Fichter and Stern, *Helv. Chim. Acta*, 1928, **11**, 1256.
[9] Wagner, *Proc. Chem. Soc.*, 1959, 229.

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detect carbonyl or oxalyl chloride which would have been formed in two other methods of decomposition.

Experiments with several iodonium salts and equivalent quantities of *N*-acetyl-3,5-dichloro-L-tyrosine ethyl ester and sodium methoxide showed the advantage of using a soluble iodonium salt. Under the same conditions the yields of pure dichloro-, dibromo-, and di-iodo-thyronine were similar, but *N*-acetyl-3-fluoro-5-iodo-DL-tyrosine ethyl ester, even with an excess of the iodonium salt, gave a lower yield (36%) of the *O*-methyl-thyronine, and *N*-acetyltyrosine ethyl ester and its 3-nitro- and 3,5-dinitro-derivatives gave no thyronine. Hillmann [2a] reported poor yields from *N*-acetyl-3-iodo-L-tyrosine ethyl ester and the unsubstituted compound. We obtained a 4% yield of 3,5-dimethyl-DL-thronine, under forcing conditions, from the disodium salt of *N*-acetyl-3,5-dimethyl-DL-tyrosine and di-*p*-methoxyphenyliodonium bromide in dimethylformamide (in which the bromide is soluble). This low yield is probably due in part to the low reactivity of the phenol and in part to destruction of the iodonium salt. In the thyronine series, therefore, the iodonium-salt route is at present virtually limited to the preparation of 3,5-dihalogeno-thyronines, but it is the only convenient method for making thyronines with fluorine, or with two different halogen atoms, in ring A, and by this route the optical activity of the tyrosine is fully preserved.[2a]

The reaction was less satisfactory in the absence of an amino-acid side-chain. 2,6-Dimethylphenol with di-*p*-methoxyphenyliodonium sulphate gave small amounts of unidentified compounds that, separated by chromatography, showed carbonyl absorption (1714 and 1704 cm.$^{-1}$) and formed derivatives with 2,4-dinitrophenylhydrazine. In the 4-*p*-hydroxyphenoxyacetic acid series the reaction gave a lower yield than does the pyridinium salt method;[10] 3,5-dichloro-4-*p*-hydroxyphenoxyphenylacetic acid was obtained in only 23% yield from ethyl 3,5-dichloro-4-hydroxyphenylacetate, and the reaction failed completely with the corresponding dibromo-compound.

The preparation of 3-chloro-5-iodo-D-thyronine (the first thyronine with different halogens in ring A to be described) is of interest. We thought it unlikely that 3-chloro-5-iodo-L-thyronine would undergo inversion in the usual way, for 3,5-dichloro-L-thyronine, when treated with nitrosyl bromide, gave an α-bromo-acid from which 3,5-dichloro-L-thyronine was obtained on ammonolysis.[11] We therefore started with D-tyrosine. Partial chlorination with sulphuryl chloride and then iodination with iodine monochloride gave the chloro-iodo-tyrosine which was converted into the thyronine in good yield.

3-Fluoro-DL-tyrosine was prepared by chloromethylating *o*-fluoroanisole and treating the benzyl chloride produced with diethyl acetamidomalonate, with final decarboxylation and hydrolysis. With iodine in ethylamine it gave 3-fluoro-5-iodo-DL-tyrosine, which was converted into the corresponding thyronine. 3,5-Dimethyl-DL-tyrosine was obtained by chloromethylating 2,6-dimethylanisole and condensing the product with diethyl acetamidomalonate, then refluxing the ester with hydriodic acid. We were not able to chloromethylate 2,6-dimethylphenyl carbonate. Other methylated phenol carbonates have, however, been chloromethylated.[12]

Experimental

M. p.s are corrected.

Di-p-*methoxyphenyliodonium Sulphate*.—Di-*p*-methoxyphenyliodonium bromide [4] (8·40 g.) was moistened with ethanol and suspended in water (50 ml.), then shaken for 1¼ hr. with silver sulphate (3·12 g.). Silver bromide was removed and the filtrate evaporated under reduced pressure, leaving the *sulphate* (7·61 g., 92%) as a colourless, amorphous mass (Found: C, 42·45; H, 3·6; I, 30·0. $C_{26}H_{28}I_2O_8S,H_2O$ requires C, 42·2; H, 3·8; I, 30·6%).

Di-p-*methoxyphenyliodonium Chloride*.—Treatment of the sulphate (5·0 g.) in water (15 ml.)

[10] Meltzer, Lustgarten, and Fischman, *J. Org. Chem.*, 1957, **22**, 1577.
[11] Warburton, following paper.
[12] Sommelet and Marszah, *Compt. rend.*, 1934, **198**, 2256.

with sodium chloride (0·75 g.) in water (10 ml.) gave the chloride as colourless needles (3·8 g., 79%), m. p. 190—191°. One crystallization from ethanol gave needles, m. p. 198—199° (Found: C, 45·0; H, 4·0; Hal., 43·1. Calc. for $C_{14}H_{14}ClIO_2$: C, 44·45; H, 3·75; Hal., 43·1%).

*Di-*p*-methoxyphenyliodonium Trichloroacetate.*—Nitric acid (5·4 ml.; *d* 1·5) was added to stirred acetic anhydride (14 ml.) at −20°. Trichloroacetic acid (20 g.) and iodine (5·0 g.) were added at room temperature. The mixture was shaken for 1 hr., then evaporated at <50° under reduced pressure. Acetic anhydride (30 ml.) was added to the residue at room temperature, followed, at −10°, by anisole (17·4 ml.), trichloroacetic acid (20 g.), and acetic anhydride (70 ml.). The mixture was kept at 0° overnight, then at room temperature for 2 days. Most of the solvent was removed under reduced pressure and ether (250 ml.) added. The yellow solid (13 g.) which separated was stirred with warm ether, leaving di-*p*-methoxyphenyliodonium trichloroacetate as colourless crystals (11·9 g., 58%), m. p. 92—93°. The compound was not obtained analytically pure. It did not give a precipitate with silver nitrate and showed strong absorption in Nujol at 1660 cm.$^{-1}$ (trichloroacetate).

*Decomposition of Di-*p*-methoxyphenyliodonium Trichloroacetate.*—The trichloroacetate (1·0 g.) was refluxed in benzene (35 ml.) for 5 min., giving the colourless chloride (0·69 g., 92%), m. p. 195—197° (decomp.). Recrystallization from ethanol gave well-formed crystals, m. p. and mixed m. p. 197—198°, identical (infrared) with an authentic sample (Found: C, 44·7; H, 3·8; Hal, 42·8. Calc. for $C_{14}H_{14}ClIO_2$: C, 44·45; H, 3·75; Hal, 43·1%). There was no absorption at 1660 cm.$^{-1}$ in Nujol, and the compound gave a precipitate with silver nitrate. Addition of potassium iodide gave the iodonium iodide, identical (infrared) with a sample prepared by known methods.[5]

*Reaction of Di-*p*-methoxyphenyliodonium Sulphate with* N*-Acetyl-3,5-dichloro-*L*-tyrosine Ethyl Ester.*—*N*-Acetyl-3,5-dichloro-L-tyrosine ethyl ester (2·00 g.), di-*p*-methoxyphenyliodonium sulphate (2·43 g.), sodium methoxide (0·338 g.), and dry methanol (30 ml.) were refluxed for 1¼ hr. *p*-Iodoanisole was removed by steam-distillation and the residue extracted with warm benzene. The extract was washed with water, dried ($MgSO_4$), and evaporated under reduced pressure, leaving an oil (2·54 g., 95%). This was refluxed for 2 hr. with acetic acid (27 ml.), constant-boiling hydriodic acid (85 ml.), and red phosphorus (2·0 g.). The mixture was filtered hot through kieselguhr and evaporated to dryness under reduced pressure. The residue was dissolved in a small volume of hot water containing a little ethanol, and a hot solution of sodium acetate containing a little sodium hydrogen sulphite was added to the boiling solution until the pH was about 5. The mixture was cooled and 3,5-dichloro-L-thyronine separated as colourless needles (1·11 g., 52%), m. p. 247—248° (decomp.) identical (infrared) with a specimen prepared by the pyridinium salt method.[11]

The effect of varying the iodonium salt is shown in the following Table; other details are as just described.

Iodonium salt	Yield of crude ester (%)	Yield of pure amino-acid (%)	Iodonium salt	Yield of crude ester (%)	Yield of pure amino-acid (%)
Iodide	0	—	Trifluoroacetate...	80	45
Bromide	Trace	—	Chloride	85	41
Sulphate	95	52	Trichloroacetate	13	Not prepared

Overall yields are not increased by purifying the ester. In dimethylformamide, under the same conditions, the bromide gave a 9% yield of the ester, but the iodide did not react.

Reaction of the N*-Acetyltyrosine Ethyl Esters with Di-*p*-methoxyphenyliodonium Sulphate.*—A series of experiments (iodonium sulphate in methanol) in which the *N*-acetyl-ester was varied is shown in the next Table; other details are as just described:

N-Acetyltyrosine Et ester	Yield of crude ester (%)	Yield of pure amino-acid (%)	*N*-Acetyltyrosine Et ester	Yield of crude ester (%)	Yield of pure amino-acid (%)
3,5-Dichloro	95	52	3-Fluoro-5-iodo ...	>100	36 *
3,5-Dibromo	96·5	58·5	3-Nitro	0	—
3,5-Di-iodo	95	47	3,5-Dinitro	0	—
3-Chloro-5-iodo ...	—	54·5	Unsubst.....	0	—

* *O*-Methylamino-acid; excess of iodonium salt used.

N*-Acetyl-3,5-dichloro-*L*-tyrosine.*—A solution of 3,5-dichloro-L-tyrosine [13] (25·0 g.) in 2N-sodium hydroxide (200 ml.) was treated with acetic anhydride (12·5 ml.) with stirring at 20°.

[13] Zeynek, *Z. physiol. Chem.*, 1921, **114**, 275.

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The solution was stirred for 1 hr., then heated at 40° for 30 min. to decompose the excess of acetic anhydride. 5N-Hydrochloric acid was added until the solution was acid to Congo Red, and the solid (18·7 g.) recrystallized from water. N-*Acetyl*-3,5-*dichloro*-L-*tyrosine* separated as needles (16·1 g., 55%), m. p. 136—139°, $[\alpha]_D^{20}$ +83·0° (*c* 5·6 in dioxan) (Found: C, 44·1; H, 4·0; N, 4·65; Cl, 23·65. $C_{11}H_{11}Cl_2NO_4,\frac{1}{2}H_2O$ requires C, 44·0; H, 4·0; N, 4·7; Cl, 23·7%).

N-*Acetyl*-3,5-*dichloro*-L-*tyrosine Ethyl Ester*.—*N*-Acetyl-3,5-dichloro-L-tyrosine (9·0 g.), toluene-*p*-sulphonic acid (0·85 g.), ethanol (6 ml.), and chloroform (280 ml.) were refluxed under an automatic water separator for 17 hr. The cold solution was extracted with 2N-sodium carbonate, and the extract acidified, giving the pale grey *ester* (7·3 g., 74%), m. p. 138—139°. Two recrystallizations from aqueous ethanol gave m. p. 140—141° (Found: C, 48·95; H, 4·8; N, 4·3; Cl, 21·8. $C_{13}H_{15}Cl_2NO_4$ requires C, 48·8; H, 4·7; N, 4·4; Cl, 22·1%).

N-*Acetyl*-3,5-*dibromo*-L-*tyrosine Ethyl Ester*.—*N*-Acetyl-3,5-dibromo-L-tyrosine [14] was esterified as above, giving the *ester* (65%), m. p. 141—143° (Found: C, 38·2; H, 3·6; Br, 38·7. $C_{13}H_{15}Br_2NO_4$ requires C, 38·2; H, 3·7; Br, 39·0%).

N-*Acetyl*-3-*nitro*-L-*tyrosine*.—3-Nitro-L-tyrosine [15] was acetylated as described above, giving the *acetyl derivative*, m. p. 189—192° (from water) (Found: C, 49·4; H, 4·6; N, 10·5. $C_{11}H_{12}N_2O_6$ requires C, 49·3; H, 4·5; N, 10·45%).

N-*Acetyl*-3-*nitro*-L-*tyrosine Ethyl Ester*.—Esterification of the preceding compound as described above gave the *ester*, m. p. 95—97° (from ethanol) (Found: C, 52·8; H, 5·4; N, 9·75. $C_{13}H_{16}N_2O_6$ requires C, 52·7; H, 5·4; N, 9·5%).

4-*Chloromethyl*-2,6-*dimethylanisole*.—A stirred mixture of 2,6-dimethylanisole (40 g.), 38% aqueous formaldehyde (20 ml.), concentrated hydrochloric acid (10 ml.), zinc chloride (6 g.), and ether (120 ml.) was saturated with hydrogen chloride at 20—25°, then kept at room temperature for 5 days. The solution was poured into ether (200 ml.) and ice (500 g.), and the organic layer washed with 2N-sodium hydrogen carbonate and water and dried ($MgSO_4$). The ether was removed at room temperature and the residue distilled as quickly as possible from an oil-bath previously heated to 80—90°. The following fractions were collected: (i) 3·5 g., b. p. 40—80°/1 mm., n_D^{24} 1·5190, mainly 2,6-dimethylanisole; (ii) 6·2 g., b. p. 80—83°/1 mm., n_D^{24} 1·5350; (iii) 30·2 g., b. p. 83—85°/1 mm., n_D^{20} 1·5375. Fractions (ii) and (iii) were 4-chloromethyl-2,6-dimethylanisole (infrared).

Ethyl α-*Acetamido*-α-(4-*methoxy*-3,5-*dimethylbenzyl*)*malonate*.—Sodium (5·50 g.) was dissolved in ethanol (250 ml.), and diethyl acetamidomalonate (52·0 g.) added to the cooled solution. 4-Chloromethyl-2,6-dimethylanisole (43·5 g.) in ethanol (150 ml.) was added, and the solution refluxed with stirring for 6 hr. The filtrate was taken to dryness under reduced pressure and the residue dissolved in ethyl acetate (500 ml.), washed with water, dried ($MgSO_4$), and again taken to dryness. The almost colourless gum solidified and was recrystallized from aqueous methanol below 40°. The *product* (69 g., 79%) separated as plates, m. p. 97—99° (Found: C, 62·4; H, 7·7; N, 4·1. $C_{19}H_{27}NO_6$ requires C, 62·45; H, 7·4; N, 3·8%).

3,5-*Dimethyl*-DL-*tyrosine*.—The preceding ester (69 g.), acetic acid (450 ml.), and constant-boiling hydriodic acid (350 ml.) were refluxed for 7 hr., then evaporated to dryness under reduced pressure. The red oil was dissolved in water (150 ml.) and extracted with ether, which removed most of the colour. The aqueous layer was brought to pH 8 with concentrated ammonia solution, washed with ethyl acetate, and concentrated under reduced pressure. 3,5-Dimethyl-DL-tyrosine was collected after refrigeration [23·1 g., 58%; m. p. 242—248° (decomp.) (lit.,[16] 250—253°)].

N-*Acetyl*-3,5-*dimethyl*-DL-*tyrosine*.—3,5-Dimethyl-DL-tyrosine (22 g.) in 2N-sodium hydroxide (500 ml.) was treated dropwise with acetic anhydride (30 ml.) at 16—20° during 2 hr. with stirring and kept overnight. The solution was then heated to 40° for 45 min., and acidified with 10N-hydrochloric acid at below 15°, giving a colourless solid (12·0 g.), m. p. 182—184°. The mother-liquors were made strongly alkaline with 40% sodium hydroxide solution and the acetylation repeated with acetic anhydride (50 ml.). A second crop of N-*acetyl*-3,5-*dimethyl*-DL-*tyrosine* (11·0 g., total yield 86%) separated. Recrystallization from acetonitrile gave rosettes, m. p. 183—185° (Found: C, 61·9; H, 6·5; N, 5·45. $C_{13}H_{17}NO_4$ requires C, 62·1; H, 6·8; N, 5·6%).

N-*Acetyl*-3,5-*dimethyl*-DL-*tyrosine Ethyl Ester*.—Esterification of the preceding compound as

[14] De Witt and Ingersoll, *J. Amer. Chem. Soc.*, 1951, **73**, 5782.
[15] Städeler, *Annalen*, 1896, **116**, 77.
[16] Steiner and Sorkin, *Helv. Chim. Acta*, 1952, **35**, 2486.

described above gave the *ester*, m. p. 101—102° (from ethyl acetate and di-isopropyl ether) (Found: C, 64·0; H, 7·5; N, 4·8. $C_{15}H_{21}NO_4$ requires C, 64·5; H, 7·6; N, 5·0%).

*3,5-Dimethyl-*DL*-thyronine.*—*N*-Acetyl-3,5-dimethyl-DL-tyrosine (1·69 g.) was dissolved in 1·17N-methanolic sodium methoxide (11·0 ml.), the methanol removed under reduced pressure, and the residue dried at 40° for 3 hr. Anhydrous dimethylformamide (20 ml.) and di-*p*-methoxyphenyliodonium bromide (2·6 g.) were added, and the mixture was heated on the steam-bath for 4 hr. with occasional shaking. The solvent was removed under reduced pressure and the residue partitioned between ethyl acetate and water. The organic layer was extracted with 2N-sodium hydroxide, and the extract, combined with the original aqueous layer, acidified and extracted with ethyl acetate. Concentration of the ethyl acetate extract gave a light brown foam (1·80 g.), which, dissolved in ethyl acetate (10 ml.) and stored overnight at 5°, gave unchanged *N*-acetyl-3,5-dimethyl-DL-tyrosine (0·40 g., 24%). The mother-liquors were taken to dryness and the residue refluxed for 2 hr. with acetic acid (10 ml.) and constant-boiling hydriodic acid (10 ml.). Evaporation left a residue, which was dissolved in water (15 ml.). The solution was partly decolorized by treatment with sodium hydrogen sulphite solution and extraction with ether, then neutralized with ammonia and concentrated under reduced pressure until crystallization started. *3,5-Dimethyl-*DL*-thyronine* separated as pale grey crystals (80 mg., 3·8%), m. p. 210—212° (decomp.) after drying at 80° in a vacuum (Found: C, 64·4; H, 6·6; N, 4·4. $C_{17}H_{19}NO_4,H_2O$ requires C, 63·9; H, 6·6; N, 4·4%). The acid was chromatographically pure.

When two equivalents of the iodonium bromide were added in successive portions, the yield was 4·3%. Ester hydrolysis made it impossible to condense *N*-acetyl-3,5-dimethyl-DL-tyrosine ethyl ester with the iodonium bromide under forcing conditions.

*3-Chloro-*D*-tyrosine.*—Chlorination of D-tyrosine [17] by the method used by Zeynek [18] in the L-series gave *3-chloro-*D*-tyrosine* (48%), m. p. 255—256° (decomp.), $[\alpha]_D^{20}$ +26·0° (*c* 0·9 in H_2O) (Found: C, 50·7; H, 4·8; N, 6·3; Cl, 16·1. $C_9H_{10}ClNO_3$ requires C, 50·1; H, 4·7; N, 6·5; Cl, 16·4%). 3-Chloro-L-tyrosine prepared by the same method had $[\alpha]_D^{20}$ −26·2°.

*3-Chloro-5-iodo-*D*- and -*L*-tyrosine.*—3-Chloro-D-tyrosine hydrochloride (11·6 g.) was dissolved in water (73 ml.) and cooled to 10°. Iodine monochloride (9·4 g.) was warmed to 40° and a stream of dry air was drawn over it and through the solution of the hydrochloride. After 3 hr. at 10°, the hydrochloride solution was decolorized with sodium hydrogen sulphite. Concentrated hydrochloric acid (73 ml.) was added and the solid which separated overnight in the refrigerator was dissolved in a little 2N-sodium hydroxide. Neutralization with 2N-acetic acid gave *3-chloro-5-iodo-*D*-tyrosine* (12·94 g., 84%), m. p. 197—198° (decomp.). Recrystallized from water it had m. p. 201° (decomp.), $[\alpha]_D^{20}$ +10·7° (*c* 0·5 in H_2O) (Found: C, 30·8; H, 3·1; N, 3·9; I, 36·3. $C_9H_9O_3ClIN,\frac{1}{2}H_2O$ requires C, 30·8; H, 2·9; N, 4·0; I, 36·2%). *3-Chloro-5-iodo-*L*-tyrosine* prepared in the same way had m. p. 201° (decomp.), $[\alpha]_D^{20}$ −10·6° (Found: C, 31·2; H, 2·7; N, 3·8; I, 35·9%).

*N-Acetyl-3-chloro-5-iodo-*D*- and -*L*-tyrosine.*—Acetylation of the amino-acids as described earlier gave *N-acetyl-3-chloro-5-iodo-*D*-tyrosine* (92%), m. p. 117—121°, $[\alpha]_D^{20}$ −69° (*c* 0·9 in dioxan) (Found: C, 33·5; H, 3·4; N, 3·5; I, 31·9. $C_{11}H_{11}ClINO_4,\frac{1}{2}H_2O$ requires C, 33·6; H, 3·1; N, 3·6; I, 32·3%), and the corresponding L-*isomer*, m. p. 115—120°, $[\alpha]_D^{20}$ +70° (Found: C, 32·9; H, 3·3; N, 3·6%).

*N-1cetyl-3-chloro-5-iodo-*D*- and -*L*-tyrosine Ethyl Ester.*—Esterification of the acetates as described above gave *N-acetyl-3-chloro-5-iodo-*D*-tyrosine ethyl ester* (85%), m. p. 127—129°, $[\alpha]_D^{20}$ −45° (*c* 0·9 in dioxan) (Found: C, 37·9; H, 3·7; N, 3·1; I, 30·8. $C_{13}H_{15}ClINO_4$ requires C, 37·9; H, 3·7; N, 3·4; I, 30·8%), and the corresponding L-isomer, m. p. 129·5—131·5°, $[\alpha]_D^{20}$ +47°.

*3-Chloro-5-iodo-*D*- and -*L*-thyronine.*—*N*-Acetyl-3-chloro-5-iodo-D-tyrosine ethyl ester (10·0 g.), di-*p*-methoxyphenyliodonium sulphate (10·6 g.), dry methanol (140 ml.), and sodium methoxide (1·32 g.) were refluxed for 1½ hr. The mixture was steam-distilled and the residue extracted with benzene, giving an oil (12·1 g.). Demethylation and purification, as described earlier, gave *3-chloro-5-iodo-*D*-thyronine* (5·81 g., 54·5%), m. p. 232—234° (decomp.), $[\alpha]_D^{20}$ −27·2° (*c* 0·7 in 1 : 1 EtOH–N-HCl) (Found: C, 39·9; H, 3·3; N, 2·9. $C_{15}H_{13}ClINO_4,\frac{1}{2}H_2O$ requires C, 39·9; H, 3·3; N, 3·1%). The corresponding L-*amino-acid* had m. p. 232—234°, $[\alpha]_D^{20}$ +27·5° (Found: C, 39·6; H, 3·4; N, 3·0%).

[17] Sealock, *Biochem. Prep.*, 1949, Vol. I, p. 71.
[18] Zeynek, *Z. physiol. Chem.*, 1925, **144**, 246.

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3,5-*Dichloro*-4-*hydroxyphenylacetic Acid.*—*p*-Hydroxyphenylacetic acid (20·0 g.) in acetic acid (750 ml.) was treated with chlorine until the temperature, which had risen to 40°, started to fall. The solution was evaporated to dryness under reduced pressure and left a residue (23·2 g.), m. p. 160°, which was washed with water and dried. Crystallization from aqueous acetic acid, then from water (charcoal), gave 3,5-*dichloro*-4-*hydroxyphenylacetic acid* (8·2 g., 29%), m. p. 176—180° (Found: C, 43·5; H, 2·8; Cl, 31·8. $C_8H_6Cl_2O_3$ requires C, 43·5; H, 2·7; Cl, 32·1%).

Esterification gave the *ethyl ester*, m. p. 78—79° (from light petroleum) (Found: C, 48·3; H, 4·1; Cl, 28·35. $C_{10}H_{10}Cl_2O_3$ requires C, 48·3; H, 4·0; Cl, 28·5%).

3,5-*Dichloro*-4-p-*hydroxyphenoxyphenylacetic Acid.*—(a) *By the iodonium salt method.* Ethyl 3,5-dichloro-4-hydroxyphenylacetate (6·0 g.), di-*p*-methoxyphenyliodonium sulphate (9·9 g.), sodium methoxide (1·41 g.), and dry methanol (90 ml.) were refluxed for 1½ hr. After steam-distillation the residue was extracted into ether, and the crude, dried product treated with hydriodic acid as above. 3,5-Dichloro-4-*p*-hydroxyphenoxyphenylacetic acid (1·75 g., 23%) separated from ethanol containing a little benzene, had m. p. 192—194°, and was identical (infrared) with the product described below.

(b) *By the pyridinium salt method.* The tetrazonium sulphate solution prepared [10] from 3,5-diamino-4-*p*-methoxyphenoxyphenylacetic acid (13·2 g.) was added slowly to a stirred mixture of cuprous chloride (23 g.), 10N-hydrochloric acid (375 ml.), and chloroform (400 ml.). The mixture was then stirred vigorously for 1 hr. Water (500 ml.) was added, the organic layer separated, and the aqueous layer extracted with more chloroform. The combined chloroform extracts were washed with water, dried (Na_2SO_4), and evaporated. The residue was dissolved in cold benzene. A dark impurity was removed by adding a little light petroleum and decanting the liquid, and evaporation left a solid, which was recrystallized from 90% aqueous acetic acid, giving 3,5-*dichloro*-4-p-*methoxyphenoxyphenylacetic acid* (7·0 g., 52%), m. p. 116·5—117·5° (Found: Cl, 20·8. $C_{15}H_{12}Cl_2O_4$ requires Cl, 21·6%).

The methoxy-compound (10·0 g.) with constant-boiling hydriodic acid (20 ml.) in acetic acid (30 ml.) containing red phosphorus (2 g.) for 16 hr. gave 8·4 g. of a crude product which was recrystallized twice from acetonitrile, giving 3,5-*dichloro*-4-p-*hydroxyphenoxyphenylacetic acid* (3·82 g.), m. p. 192—194° (Found: C, 53·7; H, 3·2; Cl, 22·8. $C_{14}H_{10}Cl_2O_4$ requires C, 53·8; H, 3·2; Cl, 22·7%).

Ethyl α-Acetamido-α-(3-fluoro-4-methoxybenzyl)malonate.—Sodium (17·0 g.) was dissolved in dry ethanol (780 ml.). Diethyl acetamidomalonate (180 g.) was added and dissolved, then 3-fluoro-4-methoxybenzyl chloride [19] (129 g.) was added with stirring. The solution was refluxed for 5 hr., then filtered hot. The solution deposited colourless crystals (172 g.), m. p. 123—125°; recrystallized material from the concentrated mother-liquors amounted to 51·0 g. Further recrystallization from ethanol gave the *ester*, m. p. 127—128° (Found: C, 57·7; H, 6·1; N, 4·0. $C_{17}H_{22}FNO_6$ requires C, 57·5; H, 6·2; N, 3·9%).

3-*Fluoro*-DL-*tyrosine.*—The preceding compound (10·0 g.), constant-boiling hydriodic acid (57 ml.), and acetic acid (57 ml.) were refluxed for 3 hr. The solution was evaporated to dryness under reduced pressure and the residue dissolved in a little hot water and decolorized with sodium hydrogen sulphite. The pH was adjusted to 5; 3-fluoro-DL-tyrosine (4·0 g., 72%) slowly separated, having m. p. 283—284° (Found: C, 54·2; H, 5·1; N, 6·6; F, 9·1. Calc. for $C_9H_{10}FNO_3$: C, 54·3; H, 5·0; N, 7·0; F, 9·6%). Kraft [19] reports m. p. 278—280°.

3-*Fluoro*-5-*iodo*-DL-*tyrosine.*—A solution of iodine (25·8 g.) in saturated potassium iodide solution (24 ml.) was added dropwise to a stirred solution of 3-fluoro-DL-tyrosine (20·0 g.) in 33% aqueous ethylamine (50 ml.). The mixture was left overnight, then most of the ethylamine was removed under reduced pressure and the pH brought to 2 with 10N-hydrochloric acid. After 24 hr. the yellow solid was washed with water and dried, giving 3-fluoro-5-iodo-DL-tyrosine (18·4 g., 56%). Recrystallization from 50% aqueous ethanol raised the m. p. to 199—201° (Found: C, 31·9; H, 2·9; I, 37·1. Calc. for $C_9H_9FINO_3,H_2O$: C, 31·5; H, 3·2; I, 37·0%). Kraft and Dergel [20] report m. p. 190—193°. We were not able to prepare this compound by Kraft and Dergel's method.

N-*Acetyl*-3-*fluoro*-5-*iodo*-DL-*tyrosine.*—Acetylation of the amino-acid as above gave an almost quantitative yield of the *acetyl derivative*, m. p. 210—214° (Found: C, 36·2; H, 3·1. $C_{11}H_{11}FINO_4$ requires C, 35·9; H, 3·0%).

[19] Kraft, *Chem. Ber.*, 1951, **84**, 150.
[20] Kraft and Dergel, G.P. 895,292.

Esterification gave the *ethyl ester* (90% yield), m. p. 172—179° (Found: C, 39·7; H, 4·0; I, 31·6. $C_{13}H_{15}FINO_4$ requires C, 39·5; H, 3·8; I, 32·2%).

3-*Fluoro*-5-*iodo*-4-p-*methoxyphenoxy*-DL-*phenylalanine*.—*N*-Acetyl-3-fluoro-5-iodo-DL-tyrosine ethyl ester (10·7 g.), di-*p*-methoxyphenyliodonium sulphate (24·2 g.), sodium methoxide (2·06 g.), and dry methanol (200 ml.) were refluxed for 18 hr. under anhydrous conditions. After steam-distillation the product was extracted into warm benzene, and the benzene extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residual red oil (14·2 g.) was refluxed with 2N-hydrochloric acid (100 ml.) and acetic acid (100 ml.) for 2 hr. Charcoal was added and boiling continued for 5 min. The solution was filtered hot, the volume reduced to *ca.* 70 ml., and the solution allowed to cool. The hydrochloride (6·3 g.) which separated was dissolved in 0·5N-sodium hydroxide (100 ml.) and neutralized at the b. p. with glacial acetic acid. 3-*Fluoro*-5-*iodo*-4-p-*methoxyphenoxy*-DL-*phenylalanine* (4·8 g., 36%) separated, having m. p. 225—228° (Found: C, 44·8; H, 3·6; N, 3·1; I, 29·2; F, 4·3. $C_{16}H_{15}FINO_4$ requires C, 44·6; H, 3·4; N, 3·2; I, 29·5; F, 4·4%).

3-*Fluoro*-5-*iodo*-DL-*thyronine*.—*N*-Acetyl-3-fluoro-5-iodo-DL-tyrosine ethyl ester (1·5 g.), di-*p*-methoxyphenyliodonium sulphate (2·0 g.), sodium methoxide (234 mg.), and dry methanol (25 ml.) were refluxed for 2 hr. After steam-distillation the product was extracted into hot benzene and the extracts were evaporated to dryness. The residual oil (1·2 g.) was refluxed for 2 hr. with 48% hydrobromic acid (20 ml.) and acetic acid (20 ml.). The solution was evaporated to dryness under reduced pressure, the residual oil dissolved in hot water, and the solution neutralized with sodium acetate solution. The amino-acid (0·26 g., 14%) recrystallized as its hydrochloride from 2N-hydrochloric acid. The hydrochloride was dissolved in 0·5N-sodium hydroxide and neutralized at the b. p. with glacial acetic acid. 3-*Fluoro*-5-*iodo*-DL-*thyronine* slowly separated as colourless crystals, m. p. 239—242° (Found: C, 41·6; H, 3·5; N, 3·0; I, 32·1; F, 5·1. $C_{15}H_{13}FINO_4$ requires C, 41·4; H, 3·4; N, 3·2; I, 29·2; F, 4·4%).

GLAXO LABORATORIES LTD.,
GREENFORD, MIDDLESEX.

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519. *The Synthesis of Thyroxine and Related Compounds. Part XVI.*[1] *The Preparation of* 3,5-*Dichloro*-D-*thyronine: an Unexpected Walden Inversion.*

By W. K. WARBURTON.

When 3,5-dichloro-L-tyrosine (I) is treated with "nitrosyl bromide" the amino-group is replaced by bromine; the resulting α-bromo-acid (II) is reconverted into the L-amino-acid (I) by ammonia. Kinetic studies have shown that there is Walden inversion at each stage. With 3,5-dinitro-L-tyrosine (IV), however, inversion occurs only during ammonolysis.

In the same reactions 3-chloro-5-nitro-L-tyrosine gives a mainly racemic product, but *O*-methyl-3,5-dichloro-L-thyronine is inverted.

3,5-DICHLORO-D-THYRONINE (IX) was required for study of its biochemical effects, but proved difficult to prepare in good yield. It can be made by methods similar to those used for 3,5-di-iodo-D-thyronine,[2] but the double Sandmeyer reaction involved proceeds poorly. 3,5-Dichloro-L-thyronine has been prepared by the iodonium-salt route,[1] and 3,5-dichloro-D-thyronine (IX) could presumably be made in the same way from *N*-acetyl-3,5-dichloro-D-tyrosine ethyl ester; but attempts to prepare 3,5-dichloro-D-tyrosine by inverting the easily obtained L-isomer unexpectedly failed.

Elks and Waller [2] converted 3,5-dinitro-L-tyrosine (IV) into the α-bromo-acid (V) (which they assumed to be the L-form) and by ammonolysis obtained 3,5-dinitro-D-tyrosine from it. When the same reactions were applied to 3,5-dichloro-L-tyrosine, the configuration was unchanged overall.

[1] Part XV, preceding paper.
[2] Elks and Waller, *J.*, 1952, 2366.

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To decide whether there had been no inversion or two inversions required kinetic evidence. Neither step was suitable for direct kinetic study, but the problem was solved by preparing the azido-acid (III) under kinetically controlled conditions.[3] The azido-acid was of the L-series, for it was reduced, with slight racemization, by chromous chloride (catalytic hydrogenation was unsuccessful) to the L-amino-acid (I). It was formed from the bromo-acid (II) in an S_N2 reaction, for, when equivalent quantities of the bromo-acid and sodium azide were allowed to react in dilute (0·2M) solution, the plot of t against $1/(a - x)$, but not that of t against log $(a - x)$, was linear over the range studied (about 85% of the reaction) ($k_2 = 2{\cdot}0 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$ in water at 35°). Therefore the azidolysis had proceeded with inversion, the bromo-acid (II) had the D-configuration, and the ammonolysis had also involved inversion. No other inversion of an α-amino-acid by a " nitrosyl halide " has been reported.

A similar kinetic study of the azidolysis of the α-bromo-acid (V) derived from 3,5-dinitro-L-tyrosine (IV) showed that the reaction was bimolecular over the range studied (about 65% of the reaction) ($k_2 = 2{\cdot}3 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$ in water at 40°). This azido-acid, however, was reduced by hydrogen bromide [4] to the D-amino-acid (reduction with chromous chloride, sodium borohydride, or hydrogen was not successful). The bromo-acid was therefore of the L-series, as Elks and Waller [2] had assumed.

Molecular-rotation differences (see Table; dioxan solutions), as well as kinetic data, indicate that the bromo-acid (II) is of the D-series.

Compound	$[M]_D^{20}$	Compound	$[M]_D^{20}$
N-Acetyl-3,5-dichloro-L-tyrosine	+275°	*N*-Acetyl-2,5-dinitro-L-tyrosine	+39°
Acid (II)	−90	Acid (V)	−92

In the dinitro-series, therefore, the difference between the molecular rotations of the acetamido- and the bromo-acid is +131°. In the dichloro-series the corresponding difference is +365°, whereas the corresponding sum is +185°. The bromo-acids are therefore probably of opposite configuration.

3,5-Dichloro-D-thyronine (IX) was also made, but in poor yield, from *O*-methyl-3,5-dichloro-L-thyronine by inversion through the bromo-acid and demethylation. The bromo-acid was not obtained analytically pure. The Sandmeyer reaction still affords the best route to compound (IX).

3-Chloro-5-nitro-L-tyrosine with " nitrosyl bromide " gave an α-bromo-acid of low optical activity. This was converted into an amino-acid,* which was partly racemic but predominantly of the L-series.

The configuration of the bromo-acid (II) is proved by the kinetic studies reported, but the molecularity of the reaction in which it is formed is not so certain. It is nevertheless highly probable that this reaction is of the S_N2 type, for complete inversion has never been observed to accompany an S_N1 reaction, and on theoretical grounds [5] is not to be expected. On the other hand, complete retention is consistent only with an S_N1 or S_Ni reaction,† and the conversion of 3,5-dinitro-L-tyrosine into its corresponding α-bromo-acid must be of one of these types. Both ammonolyses are almost certainly S_N2 reactions.

It is not easy to understand why 3,5-dichloro- and 3,5-dinitro-L-tyrosine should differ in their reaction with " nitrosyl bromide." Related amino-acids that have been inverted are: L-phenylalanine,[6] *O*-methyl-L-tyrosine,[7] *O*-methyl-3,5-dichloro-L-thyronine, and

* The rotations of substituted tyrosines are small, and conclusions in this paper are based on the much larger rotations of *N*-acetyl- or *ON*-diacetyl-tyrosines.

† I thank a Referee for suggesting the S_Ni mechanism.

[2] Cf. Brewster, Hiron, Hughes, Ingold, and Rao, *Nature*, 1950, **166**, 178; Hiron and Hughes, *J.*, 1960, 795.

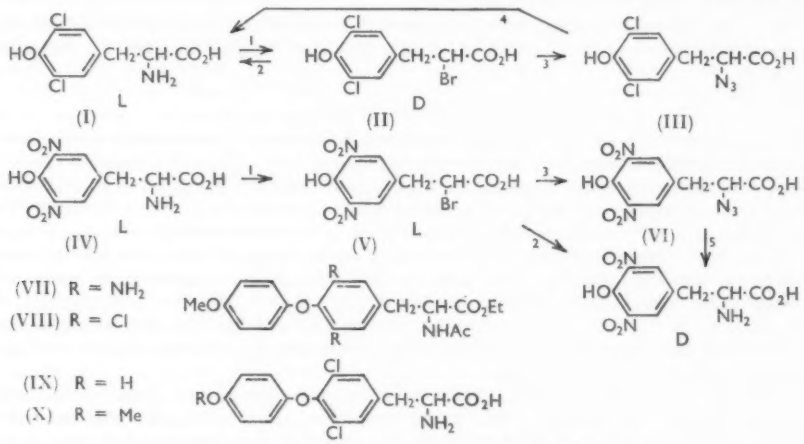
[4] Cf. Smith and Brown, *J. Amer. Chem. Soc.*, 1951, **73**, 2438.

[5] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, **1953**, pp. 381—382.

[6] Fischer and Carl, *Ber.*, 1906, **39**, 3996.

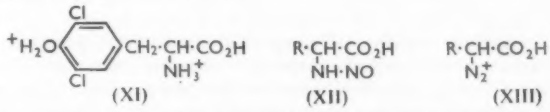
[7] Pitt-Rivers and Lermann, *J. Endocrinol.*, 1948, **5**, 223.

3,5-dinitro-L-tyrosine. 3-Chloro-5-nitro-L-tyrosine probably reacts by both the S_N1 and the S_N2 mechanism simultaneously, and the one reaction that is entirely exceptional in its steric results is that of 3,5-dichloro-L-tyrosine. This is also the only compound of those named with a relatively free *p*-hydroxyl group, a group that is absent from L-phenylalanine, bound in an ether linkage in *O*-methyl-L-tyrosine and *O*-methyl-3,5-dichloro-L-thyronine, and strongly hydrogen-bonded in 3,5-dinitro-L-tyrosine.* Although the conjugate acid (XI) could have been present only in small concentration in the 3N-sulphuric acid in which the nitrosyl bromide was generated, it could nevertheless have been the species through which the S_N2 reaction occurred. Deamination, an S_N1 reaction,[9] proceeds through the



Reagents: 1, " NOBr." 2, NH_3. 3, NaN_3 (S_N2). 4, $CrCl_2$. 5, HBr.

nitrosamine (XII), which is attacked by a proton to give the diazonium ion (XIII). The latter decomposes to a carbonium ion, which then combines with, *e.g.*, bromide ion. However, the inductive effect of a positively charged group in the *para*-position would probably make the nitrosamino-group less liable to attack by a proton. The S_N1 path would then be closed, and the reaction would be able to proceed only by the S_N2 route, with simultaneous entry of a bromide ion and expulsion of a nitrosamino-ion; this would then combine with a proton to give nitrogen and water.



Whatever the explanation of the difference in behaviour between 3,5-dichloro- and 3,5-dinitro-L-tyrosine in their reactions with " nitrosyl bromide " may be, it is likely that an S_N2 deamination for which there is no precedent has been observed. The alternative is an S_N1 (or S_Ni) reaction with complete inversion.

When 3,5-dichloro-L-tyrosine was converted into the bromo-acid (II) in more dilute (0·5N) sulphuric acid, the product was mainly the D-form, but was partly racemic.

* Infrared measurements in bromoform solution show that intramolecular hydrogen bonding is very strong in *N*-acetyl-3,5-dinitro-L-tyrosine ethyl ester [8] ($\nu_{max.}$ 3200—3100 cm.$^{-1}$), but negligible in the corresponding dichloro-compound ($\nu_{max.}$ 3580 cm.$^{-1}$). In *N*-acetyl-3-chloro-5-nitro-L-tyrosine ethyl ester ($\nu_{max.}$ 3220 cm.$^{-1}$) it is weaker than in the dinitro- but stronger than in the dichloro-compound. The same is almost certainly true of the hydrogen bonding in the amino-acids.

[8] Chalmers, Dickson, Elks, and Hems, *J.*, 1949, 3424.
[9] Ref. 5, p. 397; see also Bunton, *Ann. Reports*, 1958, **55**, 193.

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3-Chloro-5-nitro-L-tyrosine under the same conditions gave a bromo-acid not differing significantly in rotation from one prepared in more concentrated (3N) acid.

Valine and isoleucine cannot be inverted as the free amino-acids by the usual method, but, as Neuberger has explained,[10] this is probably because there is retention at each stage.

An attempt to prepare 3,5-dichloro-D-tyrosine by three successive inversions failed. It was not possible to obtain the pure L-α-bromo-acid stereoisomeric with (II) by preparing the hydroxy-acid and treating this with phosphorus tribromide in pyridine (each of which reactions should have caused inversion), probably because there was some replacement of the phenolic hydroxyl group by bromine.

The bromo-acid (II) reacted with potassium phthalimide in dimethylformamide to give an optically inactive phthalimido-acid, which was decomposed to give 3,5-dichloro-DL-tyrosine.

Experimental

M. p.s are corrected. Rotations were measured in dioxan (*c* 1) unless otherwise stated.

D-α-*Bromo*-β-(3,5-*dichloro*-4-*hydroxyphenyl*)*propionic Acid* (II).—3,5-Dichloro-L-tyrosine [1] (20·0 g.) was dissolved in 3N-sulphuric acid and cooled, with stirring, to −12°. Potassium bromide (37·5 g.) was added, then a solution of pure sodium nitrite (12·5 g.) in water (20 ml.) during 2½ hr. at −12°. The mixture was stirred for ½ hr. more without cooling. The cream solid was washed with a little ice-cold water and dried in a neutral desiccator, leaving a poorly crystalline α-*bromo-acid* (20·0 g., 80%), m. p. 70—80°. Recrystallized from benzene–light petroleum (b. p. 100—120°) it had m. p. 85·5—86·5°, $[\alpha]_D^{20}$ −28·3° (*c* 3) (Found: C, 34·5; H, 1·7; Hal., 49·0. $C_9H_7BrCl_2O_3$ requires C, 34·5; H, 2·2; Hal., 48·1%), but was only slightly purer (infrared) than the solid of m. p. 70—80°. Preparation in 0·5N-sulphuric acid gave a bromo-acid of $[\alpha]_D^{20}$ −20° in 65% yield.

Ammonolysis of α-*Bromo*-β-(3,5-*dichloro*-4-*hydroxyphenyl*)*propionic Acid*.—The crude α-bromo-acid (4·0 g.) was dissolved in concentrated ammonia solution (80 ml.) and left in a stoppered flask for 5 days at room temperature. Most of the ammonia was then removed under reduced pressure, 2N-sodium hydroxide (12·5 ml.) was added, and the rest of the ammonia was removed at <40°. Sodium hydrogen carbonate (1·7 g.) was added, then, with stirring, acetic anhydride (1·7 ml.), and the solution was stirred for 1 hr. longer. Addition of 2N-hydrochloric acid precipitated a grey solid, which recrystallized from water (charcoal), giving *N*-acetyl-3,5-dichloro-L-tyrosine (1·5 g., 40%) as needles, m. p. and mixed m. p. 133·5—134·5°, $[\alpha]_D^{20}$ +82·0° (*c* 6) (Found: C, 43·7; H, 4·1; N, 4·85. Calc. for $C_{11}H_{11}Cl_2NO_4,\frac{1}{2}H_2O$: C, 44·0; H, 4·0; N, 4·7%) (lit.,[1] m. p. 136—139°, $[\alpha]_D^{20}$ +83·0°).

Acetylation in the presence of a large excess of sodium hydrogen carbonate (not of sodium hydroxide) with an excess of acetic anhydride gave a 40% yield of *ON*-diacetyl-3,5-dichloro-L-tyrosine, m. p. 169—172°, mixed m. p. 170—172°, $[\alpha]_D^{20}$ +83·5° (Found: C, 46·7; H, 4·0; N, 4·3. Calc. for $C_{13}H_{13}Cl_2NO_5$: C, 46·8; H, 3·9; N, 4·2%).

The *N*-acetyl derivative, and the *ON*-diacetyl derivative (preparation described below), were identical (infrared spectra) with the respective authentic derivatives.

DL-β-(3,5-*Dichloro*-4-*hydroxyphenyl*)-α-*phthalimidopropionic Acid*.—The α-bromo-acid (II) (6·24 g.) was heated at 90—95° with potassium phthalimide (12·2 g.) in pure dimethylformamide (45 ml.) for 50 min. The mixture was filtered to remove unchanged potassium phthalimide, and the pale brown filtrate poured into water (200 ml.). Phthalimide was removed by filtration, the mixture extracted with chloroform, and the chloroform extracted with 2N-sodium hydroxide. Neutralization of the sodium hydroxide solution at 0° gave a colourless solid (1·25 g.), m. p. 120—122°, which was recrystallized from ethanol to give the impure DL-α-phthalimido-acid (0·77 g., 11%), needles, m. p. 154—154·5° (Found: C, 52·8; H, 3·8. Calc. for $C_{17}H_{11}Cl_2NO_5$: C, 53·8; H, 2·9%). The phthalimido-acid was decomposed with hydrazine to give 3,5-dichloro-DL-tyrosine (m. p. 215°) in 30% yield.

L-α-*Azido*-β-(3,5-*dichloro*-4-*hydroxyphenyl*)*propionic Acid* (III).—The α-bromo-acid (II) (2·00 g.) was dissolved in water (25 ml.) containing sodium hydrogen carbonate (1·07 g.), and a concentrated solution of sodium azide (1·0 g.) in water was cautiously added. The mixture was kept at 45—50° for 2 hr. Sodium acetate (5 g.) was added and the mixture cooled to 0°.

[10] Neuberger, *Adv. Protein Chem.*, 1948, **4**, 332.

2N-Hydrochloric acid was added until the solution was acid to Congo Red. The off-white solid was collected after refrigeration and recrystallized from water (40 ml.) (charcoal), giving the *azido-acid* as needles (0·92 g., 53%), m. p. 130—135°, $[\alpha]_D^{20}$ −70° (Found: C, 39·6; H, 2·5; N, 15·3; Cl, 25·5. $C_9H_7N_3Cl_2O_3$ requires C, 39·2; H, 2·5; N, 15·2; Cl, 25·7%).

Reduction of L-α-*Azido*-β-(3,5-*dichloro*-4-*hydroxyphenyl*)*propionic Acid*.—The azido-acid (2·76 g.) was dissolved in acetone (40 ml.), and an acid 2·3N-solution (10 ml.) of chromous chloride was cautiously added, with shaking, in an atmosphere of nitrogen. After 10 min., 2N-ammonia (90 ml.) was added and the mixture filtered. The green residue was extracted with 2N-ammonia (3 × 20 ml.), and the combined filtrates were shaken with kieselguhr and filtered again. 2N-Sodium hydroxide (10 ml.) was added and the filtrate concentrated under reduced pressure to 90 ml. Sodium hydrogen carbonate (5·0 g.) was added, then acetic anhydride (5·0 ml.) was added dropwise, with stirring, at room temperature, during 1 hr. The solution was stirred for 1 hr. more, filtered, and acidified with 2N-hydrochloric acid. *ON*-Diacetyl-3,5-dichloro-L-tyrosine (1·03 g., 31%) slowly separated, having m. p. and mixed m. p. 173—174°, $[\alpha]_D^{20}$ +67° (Found: C, 46·85; H, 3·9; N, 3·9%). This compound was identical (infrared spectrum) with authentic *ON*-diacetyl-3,5-dichloro-L-tyrosine.

D-α-*Azido*-β-(4-*hydroxy*-3,5-*dinitrophenyl*)*propionic Acid* (VI).—The α-bromo-acid (V) (5·0 g.) was dissolved in water (50 ml.) containing sodium hydrogen carbonate (1·5 g.), and sodium azide (5·0 g.) in water (15 ml.) was cautiously added. The mixture was kept at 45° overnight, then ice was added and the mixture made strongly acid with 2N-hydrochloric acid. A yellow oil separated and quickly solidified. The solid (3·6 g., 81%), m. p. 130—133°, $[\alpha]_D^{20}$ −35°, was extracted with a little warm benzene, leaving a solid, m. p. 139—141°, $[\alpha]_D^{20}$ −30°. This recrystallized from benzene containing a little ethanol (charcoal), giving lemon-yellow needles of the *azido-acid*, m. p. 141—143·5° (2·3 g., 50%), $[\alpha]_D^{20}$ −30° (Found: C, 36·2; H, 2·5; N, 23·1. $C_9H_7N_5O_7$ requires C, 36·4; H, 2·4; N, 23·5%).

Reduction of D-α-*Azido*-β-(4-*hydroxy*-3,5-*dinitrophenyl*)*propionic Acid*.—The azido-acid (1·02 g.) was dissolved in glacial acetic acid (15 ml.). Phenol (530 mg.) was added, then a 30% w/v solution of hydrogen bromide in acetic acid (15 ml.). Nitrogen was evolved at once. The mixture was left at room temperature overnight, then the precipitate of 3,5-dinitro-D-tyrosine hydrobromide (0·60 g., 50%) was washed with a little cold acetic acid and dried. The hydrobromide was dissolved in 2N-sodium hydroxide (4·2 ml.), then treated with acetic anhydride (0·24 ml.). *N*-Acetyl-3,5-dinitro-D-tyrosine separated on acidification, and recrystallized from 50% ethanol (7 ml.), giving pale yellow needles (230 mg., 43%), m. p. and mixed m. p. 216—217°, $[\alpha]_D^{20}$ −13·3° (Found: C, 42·4; H, 3·6; N, 13·5. Calc. for $C_{11}H_{11}N_3O_8$: C, 42·2; H, 3·5; N, 13·4%). This compound, which is dimorphic, was identical (infrared) with *N*-acetyl-3,5-dinitro-D-tyrosine, for which Elks and Waller [2] reported m. p. 192—194° (uncorr.), $[\alpha]_D^{20}$ −12·7°.

N-Acetyl-3-*chloro*-5-*nitro*-L-*tyrosine*.—3-Chloro-5-nitro-L-tyrosine [11] was acetylated as described for 3,5-dichloro-L-tyrosine, giving yellow needles (from water) of an *acid*, m. p. 184·5—185·5°, $[\alpha]_D^{20}$ +81° (Found: C, 44·0; H, 3·8. $C_{11}H_{11}ClN_2O_6$ requires C, 43·7; H, 3·6%).

The *ethyl ester* formed lemon-yellow needles (from ethanol), m. p. 129—131° (Found: C, 47·0; H, 4·55. $C_{13}H_{15}ClN_2O_6$ requires C, 47·2; H, 4·5%).

α-*Bromo*-β-(3-*chloro*-4-*hydroxy*-5-*nitrophenyl*)*propionic Acid*.—3-Chloro-5-nitro-L-tyrosine (4·0 g.) was dissolved in 3N-sulphuric acid (50 ml.) and treated with stirring, at −10° to −12°, with potassium bromide (7·5 g.), then with sodium nitrite (2·5 g.) in water (4 ml.) during 1½ hr. The pale brown oil which separated was washed with cold water and crystallized from benzene–light petroleum (b. p. 100—120°), giving the α-*bromo-acid* as lemon-yellow needles, m. p. 95—97°, $[\alpha]_D^{20}$ −17·0° (Found: C, 33·5; H, 2·2; N, 4·0; Hal, 34·5. $C_9H_7BrClNO_5$ requires C, 33·3; H, 2·15; N, 4·3; Hal, 35·5%).

Ammonolysis of α-*Bromo*-β-(3-*chloro*-4-*hydroxy*-5-*nitrophenyl*)*propionic Acid*.—The bromo-acid was decomposed with ammonia and the amino-acid acetylated as described for the dichloro-compound. N-*Acetyl*-3-*chloro*-5-*nitrotyrosine* was obtained in 30% yield, having m. p. 186·5—189·5° (decomp.), $[\alpha]_D^{20}$ +10° (Found: N, 9·1; Cl, 11·4. $C_{11}H_{11}ClN_2O_6$ requires N, 9·25; Cl, 11·75%).

Ethyl α-*Acetamido*-β-(3,5-*dichloro*-4-p-*methoxyphenoxyphenyl*)*propionate* (VIII).—Ethyl α-acetamido-β-(3,5-diamino-4-*p*-methoxyphenoxyphenyl)propionate (10 g.) was tetrazotized as described by Chalmers *et al.*[8] The tetrazonium salt was poured into a stirred solution of cuprous chloride (14 g.) in 10N-hydrochloric acid (190 ml.) containing chloroform (200 ml.). The

[11] Zeynek, *Z. physiol. Chem.*, 1925, **144**, 250.

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chloroform solution was worked up as for the di-iodo-compound,[8] and the residual gum passed in the minimum amount of cold chloroform through a column (8 × 2 cm.) of alumina. An orange gum which was eluted by chloroform was dissolved in propan-2-ol (4 ml.). Isopropyl ether was added and the solution was cooled to 0°; the ester crystallized. More isopropyl ether (6 ml.) was added and the mixture kept at 0° overnight. Filtration gave a slightly sticky solid, which was extracted with boiling cyclohexane (250 ml.) for 1 hr. The cyclohexane was decanted and the residual gum extracted again with boiling cyclohexane (200 ml.). The combined extracts were cooled slowly and refrigerated overnight, giving the *ester* (5·55 g., 50·5%), m. p. 81—83°, $[\alpha]_D^{20}$ +36° (Found: Cl, 16·0. $C_{20}H_{21}Cl_2NO_5$ requires Cl, 16·6%). In later preparations the yield seldom exceeded 40%.

3,5-*Dichloro*-L-*thyronine*.—The preceding ester (14·3 g.) was refluxed for 4 hr. with red phosphorus (10 g.), constant-boiling hydriodic acid (270 ml.), and acetic acid (100 ml.). The hot solution was filtered and, on cooling, the filtrate deposited crystals, which were collected after being cooled at 0° for 1 hr. The solid was dissolved in boiling ethanol (60 ml.) containing the minimum amount of 2N-sodium hydroxide, filtered, and treated with 20% acetic acid until the pH was 5·5. 3,5-*Dichloro*-L-*thyronine* separated as needles (6·35 g., 62%), m. p. 255° (decomp.), $[\alpha]_D^{20}$ −33° (*c* 1·0 in 1 : 1 EtOH–2N-HCl) (Found: C, 52·6; H, 3·8. $C_{15}H_{13}Cl_2NO_4$ requires C, 52·65; H, 3·8%).

ON-*Diacetyl*-3,5-*dichloro*-L-*tyrosine*.—3,5-Dichloro-L-tyrosine (3·0 g.) was dissolved in water (60 ml.) containing sodium hydrogen carbonate (4·0 g.) and 2N-sodium hydroxide (10 ml.). Acetic anhydride (4·0 ml.) was added dropwise with stirring at room temperature. After 30 min. the solution was filtered and the pH adjusted to 1 with 2N-hydrochloric acid. The solid which separated was washed with cold water and recrystallized from water (250 ml.). ON-*Diacetyl*-3,5-*dichloro*-L-*tyrosine* separated as needles (2·32 g., 58%), m. p. 171—172°, $[\alpha]_D^{20}$ +79·7° (Found: C, 46·5; H, 3·9; N, 4·1. $C_{13}H_{13}Cl_2NO_5$ requires C, 46·8; H, 3·9; N, 4·2%). This compound slowly racemizes in boiling water.

3,5-*Dichloro*-O-*methyl*-L-*thyronine*.—The ester (VIII) (10·5 g.) was refluxed in 10N-hydrochloric acid (50 ml.) and glacial acetic acid (50 ml.) for 2 hr., during which a solid separated. Water (100 ml.) was added, and the solid was collected and crystallized from pyridine (100 ml.) and water (50 ml.), giving 3,5-*dichloro*-O-*methyl*-L-*thyronine* as needles (6·05 g., 72·5%), m. p. 235° (decomp.), $[\alpha]_D^{20}$ +32° (*c* 1·0 in 1 : 1 : 1 dioxan–EtOH–2N-HCl) (Found: C, 49·1; H, 4·9; N, 3·8; Cl, 18·6. $C_{16}H_{15}Cl_2NO_4,2H_2O$ requires C, 49·0; H, 4·9; N, 3·6; Cl, 18·1%).

L-α-*Bromo*-β-(3,5-*dichloro*-4-p-*methoxyphenoxyphenyl*)*propionic Acid*.—3,5-Dichloro-*O*-methyl-L-thyronine (4·74 g.) was dissolved at 50° in a mixture of 36N-sulphuric acid (20 ml.), water (40 ml.), and glacial acetic acid (50 ml.). Potassium bromide (27·6 g.) in water (40 ml.) was added and the mixture cooled quickly, with shaking, to −5°. Sodium nitrite (9·2 g.) in water (20 ml.), cooled to 0°, was added in one portion, with shaking, to the suspension of the amino-acid in a strong 750-ml. flask. The flask was firmly stoppered and vigorously shaken behind a safety screen. The mixture was allowed to rise to room temperature (23°) and the pressure momentarily released from time to time. The total time of shaking was 2 hr. Gases were removed under reduced pressure. Water (50 ml.) was added to the pale orange solution which was then extracted with chloroform (3 × 100 ml.). The chloroform was washed with sodium hydrogen sulphite solution, then with water, dried ($MgSO_4$), and evaporated to dryness under reduced pressure, leaving a pale yellow oil which was washed with light petroleum. The residue (4·6 g., 80%), $[\alpha]_D^{20}$ −20°, did not crystallize.

3,5-*Dichloro*-O-*methyl*-D-*thyronine*.—The preceding α-bromo-acid (2·00 g.) was dissolved in concentrated ammonia solution (40 ml.) and left at room temperature in a tightly stoppered flask for 5 days. Most of the ammonia was removed under reduced pressure and 2N-hydrochloric acid added until the pH was 4·5. The resulting sticky, brown solid was washed with water and acetone, leaving a residue (650 mg., 37%), m. p. 220—222°. This was dissolved in alcoholic hydrochloric acid (charcoal) and reprecipitated with sodium acetate as almost colourless 3,5-*dichloro*-O-*methyl*-D-*thyronine* (279 mg.), m. p. 220°, $[\alpha]_D^{20}$ −25° (*c* 1·0 in 1 : 1 : 1 dioxan–EtOH–2N-HCl).

3,5-*Dichloro*-D-*thyronine* (IX).—(a) *After isolation of the methyl ether*. The crude methyl ether (145 mg.) was refluxed with red phosphorus (100 ml.), constant-boiling hydriodic acid (4 ml.), and glacial acetic acid (4 ml.) for 7 hr., then filtered while hot. The filtrate was taken to dryness and the almost colourless solid was converted into the *amino-acid* (70 mg.), m. p. 242° (decomp.), $[\alpha]_D^{20}$ −30·7° (*c* 1 in 1 : 1 EtOH–2N-HCl).

(b) *Without isolation of the ether.* The crude solid obtained by ammonolysis of the bromo-acid (4·5 g.) was drained and then refluxed with hydriodic and acetic acid for 17 hr. Removal of the acids and addition of a little sodium hydrogen sulphite, then of hot water (30 ml.), gave a colourless solution from which 3,5-dichloro-D-thyronine (600 mg., 13%), m. p. 250—252°, $[\alpha]_D^{20}$ −33° (*c* 1 in 1 : 1 EtOH–2N-HCl), was obtained on addition of sodium acetate.

Kinetic Studies.—Sodium azide was purified by crystallization from water and ethanol. Bromo-acids were of analytical purity. The extraction with chloroform described below was also done with pure 0·1N-potassium bromide. The normality found was then 0·0995N.

Azidolysis of α-bromo-β-(3,5-dichloro-4-hydroxyphenyl)propionic acid. A solution of sodium azide (650 mg.) in water (6 ml.), warmed to 35°, was added to a solution of the bromo-acid (3·140 g.) in water (25 ml.), also at 35°, containing sodium hydrogen carbonate (840 mg.). The solution was made up to 50 ml. and shaken, and the clock started. The flask was kept at 35° ± 0·1° and 3-ml. samples were drawn off at intervals and run into ice-cold 0·5N-nitric acid (4·5 ml.), then refrigerated for 48—72 hr.

Each sample was decanted from the oil or solid present, the residue was washed three times with water, and the aqueous solution extracted with chloroform (10 + 7 ml.; containing no chloride ion). The aqueous layer was boiled with 6N-nitric acid (1 ml.) until free from smell, then cooled to <25°. Saturated ferric ammonium alum solution (1 ml.) was added, followed by more 6N-nitric acid (2 ml.), then a measured volume of 0·02N-silver nitrate. The silver bromide was filtered off and the filtrate titrated with ammonium thiocyanate solution. One experiment is recorded in Table 1.

A control run in which the sodium azide was omitted showed that during 50—145 min.

TABLE 1.

Sample no.	Time (min.)	0·0235N-NH_4CNS (ml.)	0·02N-$AgNO_3$ added (ml.)	0·02N-$AgNO_3$ consumed (ml.)	$(a - x)$ (mole l.$^{-1}$)	$1/(a - x)$ (l. mole^{-1})	$\log_{10}$ $[10^3(a - x)]$
1	2·5	15·6	20	1·7	0·189	5·29	2·277
2	5	14·25	20	3·25	0·178	5·62	2·250
3	10	12·20	20	5·7	0·162	6·18	2·210
4	15	10·25	20	8·0	0·146	6·85	2·164
5	20	8·85	20	9·6	0·136	7·36	2·134
6	30	6·45	20	12·45	0·117	8·55	2·068
7	40	4·50	20	14·7	0·102	9·81	2·009
8	50	11·45	30	16·55	0·0892	11·21	1·950
9	60	10·30	30	17·9	0·0806	12·41	1·906
10	70	9·35	30	19·0	0·0727	13·75	1·862
11	80	8·85	30	19·6	0·0692	14·45	1·840
12	100	11·80	35	21·15	0·0588	17·00	1·769
13	120	10·75	35	22·4	0·0506	19·75	1·704
14	150	9·85	35	23·45	0·0433	23·1	1·637
15	175	9·00	35	24·45	0·0367	27·3	1·565
16	207	8·25	35	25·3	0·0312	32·1	1·494

TABLE 2.

Sample no.	Time (min.)	0·02N-NH_4CNS (ml.)	0·02N-$AgNO_3$ added (ml.)	0·02N-$AgNO_3$ consumed (ml.)	$(a - x)$ (mole l.$^{-1}$)	$1/(a - x)$ (l. mole^{-1})	$\log_{10}$ $[10^3(a - x)]$
1	5	19·45	20	0·55	0·196	5·10	1·292
2	10	19·05	20	0·95	0·194	5·15	1·288
3	20	8·20	10	1·80	0·188	5·32	1·274
4	30	7·50	10	2·50	0·183	5·47	1·263
5	50	6·15	10	3·85	0·174	5·75	1·241
6	70	4·90	10	5·10	0·166	6·03	1·220
7	90	3·80	10	6·20	0·159	6·30	1·201
8	120	2·20	10	7·80	0·148	6·76	1·170
9	150	1·00	10	9·00	0·140	7·15	1·146
10	180	4·75	15	10·25	0·132	7·58	1·121
11	205	3·80	15	11·20	0·125	8·00	1·097
12	235	2·80	15	12·20	0·118	8·48	1·072
13	301	1·20	15	13·80	0·108	9·27	1·033
14	360	5·10	20	14·90	0·101	9·90	1·004
15	420	3·30	20	16·70	0·088	11·40	0·945
16	480	2·30	20	17·70	0·082	12·20	0·914

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the rate of bromide-ion formation due to hydrolysis was less than 4% of that formed by azidolysis.

Azidolysis of α-bromo-β-(4-hydroxy-3,5-dinitrophenyl)propionic acid. The bromo-acid (3·35 g.) was dissolved in water (35 ml.) containing sodium hydrogen carbonate (about 1 g.) and warmed to 40°. A solution of sodium azide (650 mg.) in water (5 ml.) was warmed to 40° and added. The volume was made up to 50 ml., the flask shaken, and the clock started. The flask was kept in a water-bath at 40° ± 0·1°. Samples (3 ml.) were drawn off at intervals and run into 0·5N-nitric acid (7·5 ml.). The samples were refrigerated for 24—48 hr., then filtered. The filtrate was treated with 6N-nitric acid (3 ml.), then boiled until free from hydrazoic acid. 0·02N-Silver nitrate was added and the solutions were titrated as before. One experiment is recorded in Table 2.

A control run in which the sodium azide was omitted showed that the rate of hydrolysis was negligible.

The author thanks Professor E. D. Hughes, F.R.S., for a discussion of the reaction mechanisms.

GLAXO LABORATORIES LTD.,
GREENFORD, MIDDLESEX.

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520. *The Dissolution of Beryllium in Aqueous Solutions of Mineral Acids and Ammonium Fluoride.*

By C. J. HARDY and D. SCARGILL.

The rates of dissolution of beryllium metal in aqueous solutions of nitric, sulphuric, hydrochloric, and hydrofluoric acid, and of ammonium fluoride, have been measured and the relative rates for equimolar concentrations of the acids under similar conditions found to be $HF > H_2SO_4 \approx HCl > HNO_3$. The rate varies with the source and method of fabrication of the metal. Dissolution of beryllium in nitric acid has been examined in detail as a function of acid concentration, temperature, surface properties of the metal, and the presence of hydrofluoric acid.

METALLIC beryllium was first prepared by Wöhler [1] in 1828. Since then many conflicting statements have appeared, particularly in recent textbooks, on the dissolution of the metal in aqueous acids. All the published work has been qualitative and, since the purity of the metal has rarely been stated, impurities may account for much of the conflict in the early work.

Wöhler noted that beryllium powder, prepared by the reduction of beryllium chloride by potassium in a platinum crucible, is readily attacked by dilute hydrochloric or sulphuric acid with evolution of hydrogen, and is dissolved by cold dilute nitric acid with evolution of nitric oxide. Metal prepared by Debray,[2] by passing the chloride vapour over molten sodium, dissolved with difficulty in boiling concentrated nitric acid. Lebeau [3] found that metal produced electrolytically, in a nickel crucible, from the molten double fluoride of beryllium with sodium or potassium readily dissolved in concentrated sulphuric acid, liberating sulphur dioxide, but was only superficially attacked by concentrated nitric acid. Fichter and Jablczynski,[4] and Bodforss,[5] in work reviewed in Gmelin's "Handbuch" [6] state that freshly cleaned beryllium metal undergoes no visible attack by cold

[1] Wöhler, *Pogg. Annalen*, 1828, **13**, 577.
[2] Debray, "Du Glucinum et ses Composés," Mallet-Bachelier, Paris, 1855; *Compt. rend.*, 1854, **38**, 784; *Ann. Chim.*, 1855, **44**, 1.
[3] Lebeau, *Compt. rend.*, 1898, **126**, 744; *Ann. Chim.*, 1899, **16**, 495.
[4] Fichter and Jablczynski, *Ber.*, 1913, **46**, 1604.
[5] Bodforss, *Z. phys. Chem.*, 1926, **124**, 68.
[6] Gmelin, "Handbuch der Anorganischen Chemie," 8th edn., System-Nummer 26, "Beryllium," Verlag-Chemie, Berlin, 1930, p. 70.

concentrated nitric acid, that reaction in cold 2N-nitric acid occurs at first with evolution of gas that soon subsides, and that hot concentrated or dilute nitric acid rapidly dissolve the metal with the formation of nitric oxide and/or ammonia.

Textbooks by Mellor,[7] Remy,[8] and Sidgwick[9] contain conflicting statements on the dissolution of beryllium in nitric acid, but it appears to be generally accepted that the metal dissolves readily in sulphuric and in hydrochloric acid. We have therefore examined in detail the rate of dissolution of the purest available metallic beryllium in aqueous mineral acids, and particularly nitric acid, under a variety of conditions.

Experimental

Materials.—The beryllium metal used was in the form of sheet, tube, or disc, prepared from beryllium "flake" from the Pechiney Co. (France), or powder from the Brush Beryllium Corporation (U.S.A.). Pechiney "flake" metal is prepared by electrolysis of the mixed chlorides of beryllium and sodium at 350° in a nickel crucible as cathode with a graphite rod anode. The Brush powder is prepared by reduction of beryllium fluoride at 1300° with magnesium. The beryllium sheet was prepared by Metallurgy Division, Harwell, by powdering, sintering, and hot-rolling the Pechiney "flake" to give a laminated product 0·026" thick with a rough, dark grey surface. Beryllium tube was prepared by the Research and Development Branch, Springfields Works, U.K.A.E.A., from Pechiney powdered "flake" or Brush powder by loose-sintering into billets and extrusion into tubes of 0·3" internal diameter and 0·04" wall thickness. The surfaces were dark grey and rough with longitudinal striations. Two batches of tube produced at different times from Brush powder were examined: they are designated A and B below. The beryllium discs were made from Pechiney "flake" by vacuum-melting in a beryllia crucible, casting into an alumina-lined vessel, and extrusion into bars from which the discs were cut (2·44" in diameter × 0·635" thick; surface area 14·2 cm.²; 5·4 g.) after removal of surface scale.

Impurities in random samples of the beryllium tube determined by mass-spectrometry by R. & D.B., Springfields Works, U.K.A.E.A., in p.p.m. (except oxygen in % w/w) were as tabulated.

The beryllium sheet contained Cl, ~1100, and Fe, 300—400 p.p.m., and the beryllium discs had approximately the same specification as the Pechiney tube.

Impurity	O_2 (%)	Fe	Al	Cl	F	Si	Mn	Ni	N	H	Mg	B	Ag	Carbon combined	Carbon free
Pechiney	0·45 ± 0·09	485	705	<30	90	30	15	45	50	210	<50	—	—	255	210
Brush A	0·50 ± 0·09	800	950	30	50	1020	115	120	95	135	185	0·66	5	315	40
Brush B	0·25 ± 0·05	1100	800	—	90	225	—	—	100	90	350	—	—	365	45

Solutions of nitric, sulphuric, hydrochloric, and hydrofluoric acids were prepared by dilution of "AnalaR" acids with demineralised distilled water.

Apparatus and Procedure.—Samples of metal were dissolved in glass flasks with water-cooled condensers, except that for hydrofluoric acid Polythene vessels were used. Temperatures up to 75° were thermostatically controlled in a water-bath, and a boiling-water bath was used for experiments at 97° ± 1°. Temperatures above 100° were measured under reflux. The samples were suspended in the solutions in stainless-steel or platinum mesh cages. The amount of beryllium dissolved was determined by weighing, after washing them with water and acetone, and drying in a stream of hot air. Rates of dissolution were calculated in mg. $cm.^{-2}$ $min.^{-1}$ based on the initial geometrical surface area measured by steel rule and micrometer. All the experiments refer to dissolution in an unstirred system. However, a sample of Pechiney beryllium tube gave an identical dissolution rate in 12M-nitric acid at 97° whether unstirred or stirred at 600 r.p.m.; hence a diffusion barrier does not appear to be set up under these conditions. A 20-fold molar excess of acid was used except where otherwise stated.

[7] Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Longmans, London, 1946, Vol. IV.
[8] Remy, "Treatise on Inorganic Chemistry," Elsevier Publ. Co., Amsterdam, 1950, p. 249.
[9] Sidgwick, "Chemical Elements and their Compounds," Oxford, 1950, Vol. I.

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Results and Discussion

Dissolution of Beryllium Sheet and Tube in Nitric Acid.—The rate of dissolution of the Pechiney beryllium sheet and Brush beryllium tube A during the first 0·5—1 hr. was usually greater than the final constant value (as shown in curve 1 of Fig. 3). This is thought to be due to the surface film or scale, and later samples of Brush beryllium tube B and Pechiney tube did not show this effect, possibly because of improved fabrication techniques. Rates of dissolution for a range of acid concentrations and temperatures are given in Tables 1 and 2, together with the initial rates and amounts dissolved before

Table 1. *Dissolution of Pechiney beryllium sheet in nitric acid.*

		Initial variable dissolution rate			Final constant dissolution rate	
HNO_3 concn. (moles/l.)	Dissn. temp.	Time (hr.)	Wt. dissolved (%)	Average rate (10^{-2} mg. cm.$^{-2}$ min.$^{-1}$)	Wt. % dissolved/hr.	Rate (10^{-2} mg. cm.$^{-2}$ min.$^{-1}$)
1	~97°	0·75	2·5	3·14	1·75	1·67
2	,,	0·75	2·0	2·54	1·75	1·67
4	,,	1·0	7·4	7·03	4·33	4·14
6	,,	1·0	8·2	7·8	5·5	5·2
8	,,	0·5	2·5	4·73	3·75	3·55
8	,,	—	—	—	6·0	5·0
10	,,	0·75	5·0	6·3	5·6	5·25
12	,,	1·0	13·0	12·2	8·0	7·53
14	,,	1·0	10·75	10·2	6·25	5·95
8	25	—	—	—	0·08	0·06
8	50	—	—	—	0·33	0·307
8	75	—	—	—	2·5	2·28
14	25	—	—	—	0·125	0·118
14	50	—	—	—	0·80	0·752
14	75	—	—	—	3·0	2·8

Table 2. *Dissolution of Brush beryllium tube A in nitric acid.*

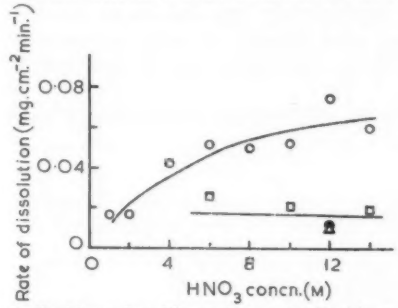
		Dissolution rate in first hour		Constant dissolution rate	
HNO_3 concn. (moles/l.)	Dissn. temp.	Wt. dissolved (%)	Average rate (10^{-2} mg. cm.$^{-2}$ min.$^{-1}$)	Wt. % dissolved/hr.	Rate (10^{-2} mg. cm.$^{-2}$ min.$^{-1}$)
6	approx. 97°	6·5	10	1·7	2·6
10	,,	5·2	7·9	1·4	2·1
14	,,	5·4	8·25	1·27	1·94
14	50	1·5	2·3	0·3	0·46
8	115 (reflux)	7·5	11·4	1·75	2·68
12	123 (reflux)	7·8	11·8	2·4	3·65

the constant rates were reached. The constant rates of dissolution of beryllium sheet and tube are plotted against the nitric acid concentration in Fig. 1 and against the temperature in Fig. 2. The constant rates for the tube are generally lower than for the sheet but follow the same trends, being approximately independent of acid concentration from 6M to 14M, and increasing markedly with temperature.

The removal of the surface film or scale was examined in an attempt to understand the difference between the initial and the final rate of dissolution, and to reduce the large amount of beryllium rapidly dissolved at high temperature and high acidity. The dissolution of an untreated Brush beryllium tube A as a function of time is compared in Fig. 3 with the dissolution of tubes treated as follows: (2) descaled with a solution 2M in nitric and 0·05M in hydrofluoric acid at 20°, and (3) chemically " polished " with chromic oxide–phosphoric acid–sulphuric acid at about 60° for 5 min., which gave a smooth, bright, silvery surface. The dissolution rates of the descaled tubes were constant from the start and almost the same as the final constant rate of the untreated tube. The mechanism of dissolution at high temperature cannot simply be an initial fast removal of scale because only 3 wt. % of the tube was removed in descaling process (2), whereas amounts up to 8%

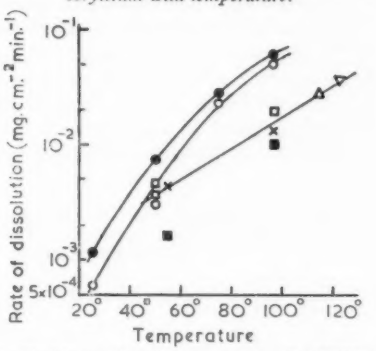
were removed at the rapid rate (Table 1) at high temperature from untreated tubes. The dissolution rate of the chemically polished tube is lower than that of the descaled tube owing to the lower acidity used in the dissolution of the former and the rougher surface of the latter. The rate of the polished sample increased slightly with time as the surface

FIG. 1. *Variation of the dissolution rate of beryllium with nitric acid concentration at 97°.*



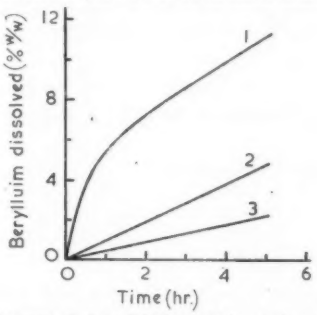
○ Pechiney beryllium sheet; ● Pechiney beryllium tube; □ Brush beryllium tube A; △ Brush beryllium tube B.

FIG. 2. *Variation of the dissolution rate of beryllium with temperature.*



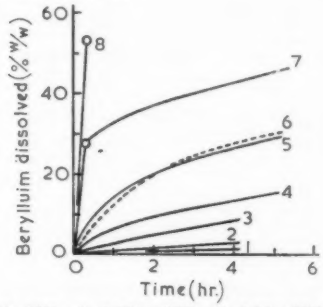
○ Pechiney beryllium sheet, 8M-HNO_3;
● Pechiney beryllium sheet, 14M-HNO_3;
× Pechiney beryllium tube, 12M-HNO_3;
■ Brush beryllium tube B, 12M-HNO_3;
△ Brush beryllium tube A, 8M-HNO_3;
▽ Brush beryllium tube A, 12M-HNO_3;
□ Brush beryllium tube A, 14M-HNO_3.

FIG. 3. *Dissolution of untreated and descaled Brush beryllium tube* A *in nitric acid.*



1, Untreated, 14M-HNO_3 at 97°. 2, Descaled in 2M-HNO_3–0·05M-HF, then 14M-HNO_3 at 97°. 3, Chemically polished, 6M-HNO_3 at 97°.

FIG. 4. *Effect of hydrofluoric acid on the dissolution of Pechiney beryllium tube in* 14M-HNO_3 *at* 50°.



1, No HF; 2, 0·001M-HF; 3, 0·01M-HF; 4, 0·05M-HF; 5, 0·1M-HF; 6, 0·01M-HF–12M-HNO_3, 97°; 7, 0·25M-HF; 8, 0·5M-HF.

○ indicates that temperature increased to near the b. p.; samples were removed for weighing after reaction abated, and solution was cooled to 50° before continuation.

became etched and pitted ($5{\cdot}8 \times 10^{-3}$ for the first hour and $6{\cdot}8 \times 10^{-3}$ mg. cm.$^{-2}$ min.$^{-1}$ after the first hour).

Effect of Hydrofluoric Acid on the Dissolution of Beryllium in Nitric Acid.—The effect of hydrofluoric acid in 14N-nitric acid at 50° on the dissolution of Pechiney beryllium tube is shown in Fig. 4. Above 0·1M-hydrofluoric acid the reaction became very vigorous and caused the temperature to rise almost to the b. p. The rate of dissolution in solutions

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containing >0·01M-hydrofluoric acid was initially fast but became constant at about 0·04 mg. cm.$^{-2}$ min.$^{-1}$. This did not occur, however, until the molar ratio Be : HF in solution exceeded 3. This effect was more pronounced at 97°, where the rate for 0·01M-hydrofluoric in 12M-nitric acid is equal to that for 0·1M-hydrofluoric acid at 50°. The reaction was very vigorous with 0·05M-hydrofluoric acid at 97°, and the temperature rapidly increased to the b. p.

Dissolution of Beryllium in Aqueous Sulphuric, Hydrochloric, and Hydrofluoric Acid.—Brush beryllium tube A dissolved rapidly in 3M-sulphuric acid at 50° with evolution of hydrogen, and the temperature rapidly increased to the b. p. The dissolution rate was 13 mg. cm.$^{-2}$ min.$^{-1}$. The reaction was also fast when started at room temperature, because the temperature also rose rapidly to the b. p. The molar ratio of acid used to beryllium dissolved was 0·75.

Samples of Pechiney beryllium tube, Brush tube B, and Pechiney discs were partially

FIG. 5. *Variation of the dissolution rate of Pechiney beryllium tube with hydrofluoric acid concentration in* 14M-HNO_3 *at* 50°.

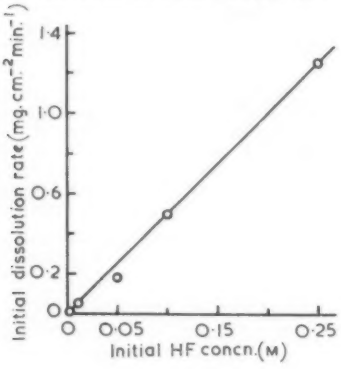
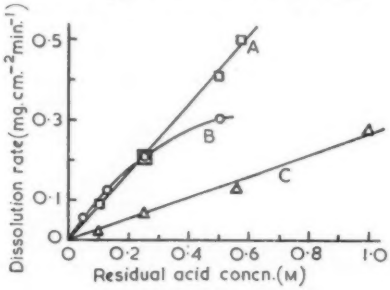


FIG. 6. *Dissolution of Pechiney beryllium discs in* N-*aqueous mineral acids at* 30—33°.



A, HF. B, H_2SO_4. C, HCl.

dissolved in N-sulphuric-, hydrochloric-, and hydrofluoric-acid at 30—33° and gave the following dissolution rates (mg. cm.$^{-2}$ min.$^{-1}$):

	Initial dissolution rate		
	1 N-H_2SO_4	1 N-HCl	1 N-HF
Pechiney tube	0·37	0·54	1·0
Brush tube B	0·24	0·16	0·8
Pechiney disc	0·31	0·28	0·8

The dissolution rate decreased linearly with decreasing acid concentration for both hydrochloric and hydrofluoric acid, but non-linearly for sulphuric acid (Fig. 6). The dissolution rate in hydrochloric acid fell to zero at the theoretical equivalence point given by the equation, $Be + 2HCl \longrightarrow BeCl_2 + H_2$, but at the equivalence point in hydrofluoric acid, dissolution continued at a constant rate of 0·03 mg. cm.$^{-2}$ min.$^{-1}$ until 0·6 g.-atom of Be had dissolved per mole of acid, and similarly in sulphuric acid until 1·15 g.-atoms had dissolved.

The differences in rate for the different samples are probably mainly due to structural differences arising in the beryllium during fabrication, since the attack by the acid caused particles to break away from the surface, giving a black suspension. The surface of the Pechiney tube was pitted to a greater extent than the surfaces of the other samples at the end of the dissolution period.

The relative rate of dissolution of a given sample of beryllium in equimolar solutions of various mineral acids under similar conditions is therefore $HF > H_2SO_4 \sim HCl > HNO_3$.

Dissolution of Beryllium in Aqueous Ammonium Fluoride.—The dissolution of Brush beryllium tube A in 5M-ammonium fluoride is fairly rapid, with evolution of hydrogen at initial rates of 0·6 and 2·4 mg. cm.$^{-2}$ min.$^{-1}$ at 50° and 97° respectively. The rate of dissolution at 50° decreases exponentially with time and approaches zero as the molar ratio of fluoride to dissolved beryllium approaches 4. However, at 97° a precipitate was formed and the final molar ratio tended towards 3. The molar ratios of dissolved beryllium, ammonium fluoride consumed, hydrogen evolved, and ammonia produced were therefore quantitatively determined as 1 : 3·96 : 0·96 : 1·9, which indicates the reaction:

$$Be + 4NH_4F + 2H_2O \longrightarrow (NH_4)_2BeF_4 + H_2 + 2NH_4{\cdot}OH$$

Since at 97° the reaction tends to go further with the formation of a precipitate, it seems probable that beryllium hydroxide is formed, thus liberating more ammonium fluoride for further attack of the beryllium, *e.g.*, $(NH_4)_2BeF_4 + 2NH_4{\cdot}OH \longrightarrow 4NH_4F + Be(OH)_2$.

CHEMISTRY DIVISION, ATOMIC ENERGY RESEARCH ESTABLISHMENT,
HARWELL, BERKS. [*Received, December 2nd,* 1960.

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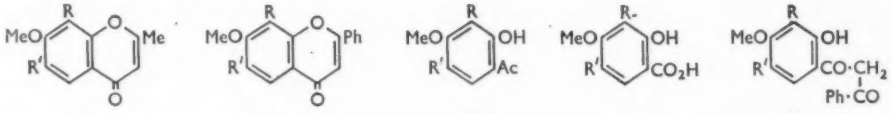
521. *Chromones and Flavones. Part III.*[1] *Synthesis of Some Cyano-chromones and -flavones.*

By M. V. SHAH and SURESH SETHNA.

Cyano-chromones and -flavones have been synthesised by the Rosenmund–von Braun reaction from the iodo-chromones and -flavones and by Kostanecki–Robinson acylation of 3- and 5-cyano-2-hydroxy-4-methoxy-acetophenone. The action of alkali and sulphuric acid on the cyano-compounds has been studied.

DA RE *et al.*[2,3] synthesised 6- and 8-cyano-2,3-dimethylchromone and 4′-cyanoflavone. No other work on the synthesis of cyano-chromones and -flavones has been reported. In the present work two iodochromones [4] (Ia and b) and an iodoflavone (IIa) were fused with cuprous cyanide (Rosenmund–von Braun reaction), affording the corresponding cyano-chromones (Ic and d) and -flavone (IIc) in good yield. These were demethylated to the corresponding hydroxy-compounds.



(I) (II) (III) (IV) (V)

	a	b	c	d
R:	I	H	CN	H
R′:	H	I	H	CN

In further work the cyano-ketones (IIIc and d) were synthesised by reaction of 3- and 5-iodo-2,4-dimethoxyacetophenone with cuprous cyanide and subsequent partial demethylation with aluminium chloride and then subjected to Kostanecki–Robinson acetylation and benzoylation. The 3-acetyl-8- and -6-cyanochromone and the benzoylflavones obtained were identical with those obtained by the Rosenmund–von Braun method. 3-Acetyl-8-cyano-7-methoxy-2-methylchromone was deacetylated to the cyanochromone (Ic) by hot alkali, but the 6-cyano-isomer gave a mixture of the cyano-ketone (IIId) and

[1] Part II, Shah and Sethna, *J.*, 1960, 3899.
[2] Da Re, *Farmaco* (*Pavia*), *Edn. Sci.*, 1956, **11**, 678.
[3] Da Re, Colleoni, and Verlicchi, *Ann. Chim.* (*Italy*), 1958, **48**, 762.
[4] Shah and Sethna, *J.*, 1959, 2676.

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TABLE 1. *Products from Rosenmund–von Braun reactions.*

No.	Substance	Reaction temp.	Product	Yield (%)	M. p.	Found (%) C	H	N	Formula	Required (%) C	H	N
1	Me ether of IIIa	165—170°	3-Cyano-	57	131°	65·0	5·2	6·6	$C_{11}H_{11}O_3N$	64·4	5·4	6·8
2	Me ether of IIIb	185—190	5-Cyano-	67	192	64·5	5·9	6·7	$C_{11}H_{11}O_3N$	64·4	5·4	6·8
3	Ia	235—240	Ic	63	262	67·0	4·3	6·8	$C_{12}H_9O_3N$	67·0	4·2	6·5
4	Ib	245—250	Id	58	249	67·5	4·1	6·3	$C_{12}H_9O_3N$	67·0	4·2	6·5
5	IIa	220—225	IIc	54	235	73·5	3·4	5·3	$C_{17}H_{11}O_3N$	73·6	4·0	5·0
			Demethylation products from compounds mentioned in column 4 above.[a]									
1	IIIc				169°	63·0	5·1	7·2	$C_{10}H_9O_3N$	62·8	4·7	7·3
2	IIId				180	62·3	4·8	7·5	$C_{10}H_9O_3N$	62·8	4·7	7·3
3	7-Hydroxy-8-cyano-2-methylchromone				368	65·2	3·5	7·2	$C_{11}H_7O_3N$	65·7	3·5	7·0
4	7-Hydroxy-6-cyano-2-methylchromone				340	65·9	3·7	7·2	$C_{11}H_7O_3N$	65·7	3·5	7·0
5	7-Hydroxy-8-cyanoflavone				315	72·9	3·9	5·2	$C_{16}H_9O_3N$	73·0	3·5	5·3

Nos. 3, 4, and 5 dissolve in sodium hydrogen carbonate solution with effervescence. No. 5 shows intense violet fluorescence with sulphuric acid.

TABLE 2. *Kostanecki–Robinson "Acetylation"* (A) *or "Benzoylation"* (B).

Ketone	Reaction	Product *	Yield (%)	M. p.	Found (%) C	H	N	Formula	Required (%) C	H	N
IIIc	A	3-Acetyl-8-cyano-7-methoxy-2-methylchromone	39	230°	65·3	4·0	5·8	$C_{14}H_{11}O_4N$	65·4	4·3	5·4
	B	3-Benzoyl-8-cyano-7-methoxyflavone	50	258	76·0	3·8	3·6	$C_{24}H_{15}O_4N$	75·6	4·0	3·7
IIId	A	3-Acetyl-6-cyano-7-methoxy-2-methylchromone	33	220	65·7	4·4	5·3	$C_{14}H_{11}O_4N$	65·4	4·3	5·4
	B	3-Benzoyl-6-cyano-7-methoxyflavone	57	281	75·0	4·3	3·8	$C_{24}H_{15}O_4N$	75·6	4·0	3·7

* Obtained also by heating the corresponding 3-acyl-6- or -8-iodo-chromone or -flavone (see Part II) with cuprous cyanide for 10 min., for chromones at 220° and for 8- and 6-iodoflavone at 250° and 285° respectively.

TABLE 3. *Products of hydrolysis by sulphuric acid.*

No.	Parent	H_2SO_4 (% by wt.)	Product *	Yield (%)	M. p.	Found (%) C	H	Formula	Required (%) C	H
1	Ic and 3-Ac of Ic	70	7-Hydroxy-2-methylchromone	—	249°	—	—	—	—	—
2	8-Cyano-7-hydroxy-2-methylchromone	95[a]	7-Hydroxy-2-methylchromone-8-carboxylic acid	36	259	59·8	4·0	$C_{11}H_8O_5$	60·0	3·7
3	Id and 3-Ac of Id	70	7-Hydroxy-2-methylchromone-6-carboxylic acid	45, 33	302	60·5	4·0	$C_{11}H_8O_5$	60·0	3·7
4	Id	50	7-Methoxy-2-methylchromone-6-carboxylic acid	36	245	61·3	4·4	$C_{12}H_{10}O_5$	61·5	4·3
5	IIc and 3-Bz of IIc	70	7-Hydroxyflavone	—	240	—	—	—	—	—
6	IIc	50	(i) 8-Carbamoyl-7-methoxyflavone[b] and	37	296	69·1	4·6	$C_{17}H_{13}O_4N$	69·1	4·4
						N, 4·9			N, 4·7	
			(ii) 7-Methoxyflavone-8-carboxylic acid	18	216	68·7	4·6	$C_{17}H_{12}O_5$	68·9	4·1
7	8-Cyano-7-hydroxyflavone	50	7-Hydroxyflavone-8-carboxylic acid	46	242	67·9	3·7	$C_{16}H_{10}O_5$	68·1	3·6
8	IId and 3-Bz of IId	70	7-Hydroxyflavone-6-carboxylic acid	50, 45	311	67·8	3·6	$C_{16}H_{10}O_5$	68·1	3·6

* Nos. 2, 4, 6 (ii), and 7 are soluble in sodium hydrogen carbonate solution with effervescence whereas Nos. 3 and 8 form a sodium salt with sodium hydrogen carbonate. Nos. 2, 3, 7, and 8 give a reddish-violet colour with alcoholic ferric chloride and melt with effervescence. Nos. 2, 3, 6 (ii), 7, and 8 were decarboxylated when heated with quinoline and copper powder, and the products were compared with authentic specimens.

[a] Heated on a steam-bath for 3 hr. [b] Yielded 7-hydroxyflavone-8-carboxylic acid when heated in acetic acid with hydriodic acid.

the acid (IVd). 3-Benzoyl-8- and -6-cyano-7-methoxyflavone, on treatment with alkali, gave the acids (IVc and d) and small quantities of the β-diketones (Vc and d) identical with those synthesised by the Baker–Venkataraman transformation of the *O*-benzoyl derivatives of the cyano-ketones (IIIc and d). The β-diketones cyclised to the cyanoflavones (IIc and d) in concentrated sulphuric acid. When the cyano-chromones and -flavones were treated with 70% sulphuric acid, demethylation, deacylation (in the case of 3-acyl compounds), and hydrolysis of the cyano-group to carboxyl occurred. In the cases (Ic) and (IIc) the cyano-group was eliminated. When 50% sulphuric acid was used no demethylation was observed.

Experimental

Rosenmund–von Braun Synthesis (*see Table* 1).—The iodo-derivative (0·01 mole) was stirred with cuprous cyanide (0·02 mole) for 10 min. at the temperature specified in Table 1. The mixture was powdered and extracted with acetone or alcohol; the product recrystallised from alcohol in needles. Addition of copper sulphate (0·001 mole) or the cyano-derivative (trace) from a previous run to the reaction mixture improved the yield.[5]

Kostanecki–Robinson "Acetylations" (*see Table* 2).—The cyano-ketone (2 g.) was heated with freshly fused sodium acetate (5 g.) and acetic anhydride (25 ml.) at 170—180° for 8 hr. The mixture was then added to cold water; the product crystallised from acetic acid (charcoal) in needles.

Kostanecki–Robinson "Benzoylations" (*see Table* 2).—The cyano-ketone (1 g.) was heated with freshly fused sodium benzoate (3 g.) and benzoic anhydride (10 g.) at 170—180° for 8 hr. The mixture was then treated repeatedly with hot water and sodium hydrogen carbonate, and the residue crystallised from acetic acid (charcoal), forming needles.

Alkaline Hydrolysis.—(*a*) 3-Acetyl-8-cyano-7-methoxy-2-methylchromone was heated with 2% alcoholic sodium carbonate solution for ½ hr. The product obtained on acidification was extracted first with sodium hydrogen carbonate solution and then with sodium hydroxide, and *3-cyano-2-hydroxy-4-methoxybenzoic acid* (IVc), m. p. 234—235° (effervescence) (Found: C, 55·9; H, 3·4; N, 7·8. $C_9H_7O_4N$ requires C, 56·0; H, 3·7; N, 7·3%), and 3-cyanopeonol (see Table 1) were isolated. The residue was the cyanochromone (Ic).

(*b*) 3-Acetyl-6-cyano-7-methoxy-2-methylchromone on similar treatment with 5% alcoholic sodium carbonate solution for 2 hr. gave *5-cyano-2-hydroxy-4-methoxybenzoic acid* (IVd), m. p. 232—233° (effervescence) (Found: C, 56·0; H, 3·7; N, 7·5%), and 5-cyanopeonol (see Table 1).

(*c*) 3-Benzoyl-8-cyano-7-methoxyflavone was refluxed with 10% alcoholic potassium hydroxide for 2 hr. The product obtained on acidification was treated with aqueous sodium hydrogen carbonate, and the cyano-phenolic acid (IVc) separated. The undissolved product, *3-cyano-2-hydroxy-4-methoxydibenzoylmethane* (Vc), crystallised from alcohol in needles, m. p. 230° (Found: C, 69·4; H, 4·5; N, 4·8. $C_{17}H_{13}O_4N$ requires C, 69·1; H, 4·4; N, 4·7%). On treatment with concentrated sulphuric acid it yielded the cyano-flavone (IIc). This β-diketone was also synthesised from *2-benzoyloxy-3-cyano-4-methoxyacetophenone* [prepared from the ketone (IIIc) by reaction with benzoyl chloride and pyridine], m. p. 182° (from alcohol) (Found: C, 69·4; H, 4·2; N, 5·1. $C_{17}H_{13}O_4N$ requires C, 69·1; H, 4·4; N, 4·7%). This ketone (2 g.) in benzene (30 ml.) was refluxed with pulverised sodium (0·3 g.) for 4 hr. and the precipitated sodium salt was decomposed with acetic acid to afford the β-diketone.

(*d*) 3-Benzoyl-6-cyano-7-methoxyflavone, on similar treatment with alcoholic potassium hydroxide, gave the acid (IVd) and *5-cyano-2-hydroxy-4-methoxydibenzoylmethane* (Vd), m. p. 204° (Found: C, 69·1; H, 4·5; N, 4·3%). This was also synthesised from *2-benzoyloxy-5-cyano-4-methoxyacetophenone* [prepared from the ketone (IIId)], m. p. 195—196° (Found: C, 69·5; H, 4·4; N, 4·2%). This ketone, when refluxed in toluene with sodium for 4 hr. and worked up as above, yielded the β-diketone.

6-Cyano-7-methoxyflavone (IId).—The above β-diketone was dissolved in concentrated sulphuric acid and kept for 4 hr. The *product*, obtained by pouring the mixture over ice, crystallised in needles, m. p. 226—227°, from alcohol (Found: C, 73·1; H, 4·3; N, 5·1. $C_{17}H_{11}O_3N$ requires C, 73·6; H, 4·0; N, 5·0%).

Sulphuric Acid Hydrolysis (*see Table* 3).—The cyano-compound (0·5 g.) was gently refluxed

[5] Cf. Koelsch and Whitney, *J. Org. Chem.*, 1941, **6**, 795.

with sulphuric acid (25 ml.), of the specified strength, for 3 hr. The product obtained by pouring the mixture on ice was treated with aqueous sodium hydrogen carbonate to separate the acid. Both the *acid* and the residue, if any, were crystallised from dilute alcohol.

Demethylations (*see Table* 1).—The cyano-ketones were partially demethylated with aluminium chloride in the dry state or by heating them in dry nitrobenzene solution on a steam-bath for 3 hr. The product obtained after steam-distillation of nitrobenzene was purified by extraction with alkali. It crystallised from alcohol in needles. The cyano-chromones and -flavones were demethylated by heating their acetic acid solutions with hydriodic acid at 120—125° for 3 hr. The mixture was poured into sodium hydrogen sulphite solution and the *product* was extracted with alkali. It crystallised as needles from acetic acid. In the case of (IId), 7-hydroxy-2-methylchromone-6-carboxylic acid was obtained by use of hydriodic acid; hence it was demethylated by aluminium chloride at 120° (3 hr.).

In general, demethylations with aluminium chloride were smooth, whereas those with hydriodic acid gave undesirable coloured products especially at reaction temperatures above 130°.

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CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE, M.S. UNIVERSITY OF BARODA, BARODA, INDIA. [*Received, December 12th*, 1960.]

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522. *The Infrared Absorption of Normal and* ^{18}O*-Labelled N-Methylbenzamide.*

By S. PINCHAS, DAVID SAMUEL, and MARTA WEISS-BRODAY.

The infrared absorptions of normal and 89 atom % *N*-methylbenz[^{18}O]-amide were measured in solution in carbon tetrachloride, chloroform, and bromoform, and as Nujol mulls, in the 3700—670 cm.$^{-1}$ region. The bands are assigned to molecular vibrations, and the origin of the characteristic secondary amide bands is discussed in the light of their location in the labelled spectra. The C=^{18}O stretching band was about 20% stronger than that due to the C=^{16}O group (in CCl_4).

THE infrared absorption of a number of various X=^{18}O compounds (X = C, P, N) was recently investigated, especially in connection with the intensities of the X=^{18}O stretching bands compared with those of the corresponding X=^{16}O bands.[1] It was observed [1d] that benz[^{18}O]amide behaves differently in showing a higher intensity for its C=^{18}O band (in CCl_4) instead of the lower intensity observed with such X=O bands [1] in the other cases studied. We have therefore investigated *N*-methylbenzamide. The infrared spectrum of normal ^{18}O-labelled methylbenzamide is also of interest from the point of view of the interpretation of the " II and III amide bands " of secondary amides, which is a matter of much controversy.[2] The spectra obtained for solutions in carbon tetrachloride, chloroform, and bromoform and for Nujol mulls, in the 3700—670 cm.$^{-1}$ region, are reported in Table 1, where the optical densities are added in parentheses.

That 0·007 g. of *N*-methylbenzamide in 1 ml. of carbon tetrachloride shows a considerable band (which disappears on further dilution) at 3350 cm.$^{-1}$ and only a weak band at about 3460 cm.$^{-1}$ is proof that in these solutions the amide exists mainly in the dimeric form; the (*trans*) secondary amides N–H stretching frequency of the dimer is known to appear at about 3350 cm.$^{-1}$, while their monomeric N–H vibration is in the 3450 cm.$^{-1}$ region.[3] With 0·7 g./l., however, the amide is practically fully in the monomeric modification,

[1] Halmann and Pinchas, *J.*, 1958, (*a*) 1703, (*b*) 3264; (*c*) 1960, 1246; Pinchas, Samuel, and Weiss-Broday, *J.*, 1961, (*d*) 1688, (*e*) 2382.

[2] See, *e.g.*, Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen & Co. Ltd., 2nd edn., London 1959, pp. 217, 218.

[3] Klemperer, Cronyn, Maki, and Pimentel, *J. Amer. Chem. Soc.*, 1954, **76**, 5846.

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as judged from the presence of only the 3470—3480 cm.$^{-1}$ band in this range of its spectrum. This value for this band seems to show that the *N*-methylbenzamide exists in its *trans*-configuration, in analogy with *N*-methylacetamide,[4] since the range for *trans*-N–H groups is usually 3440—3460 cm.$^{-1}$ while it is 3420—3440 cm.$^{-1}$ for *cis*-groups.[4] Steric interaction between the bulky methyl group and the aromatic hydrogen atoms probably contributes to stabilise further the less hindered *trans*-form of this amide.

TABLE 1. *Infrared absorption bands of normal and* ^{18}O*-labelled* N*-methylbenzamide.*

No.	Material	Solvent	Concn.	Thickness (mm.)	Bands (cm.$^{-1}$) νN–H	νN–H
1	Normal	CCl_4	0·007 g. + 1 ml.	0·5	3460(0·07)	3350(0·12)
2	89% ^{18}O	CCl_4	0·0076 g. + 1 ml.	0·5	3470(0·05)	3350(0·10)
3	Normal	CCl_4	0·3 g./l.	20	3480(0·10)	
4	89% ^{18}O	CCl_4	0·7 g./l.	20	3470(0·24)	
5	Normal	$CHCl_3$	0·0064 g./ml.	0·5	3470(0·06)	
6	89% ^{18}O	$CHCl_3$	0·0073 g./ml.	0·5	3460(0·11)	
7	Normal	$CHBr_3$	0·0077 g. + 1 ml.	0·5	[c]	
8	89% ^{18}O	$CHBr_3$	0·0093 g. + 1 ml.	0·5	[c]	

No.	νC_{ar}–H [d]	νCH_3 [g]	νC=O	$\nu(C{=}C)_{ar}$	II amide	Bands (cm.$^{-1}$) antisym. δCH_3	sym. δCH_3
1	3080(0·05)	2940(0·07)	1673(0·73)	1579(0·20)	1524(0·36)	1484(0·31)	1415(0·16)
2	3070(0·05)	2950(0·05)	1649(0·50)	1579(0·14)	1524(0·6)	1483(0·31)	1413(0·17)
3	3050(0·04)	2940(0·07)	1675(1·0) [b]				1413(0·15)
4	3050(0·22)	2940(0·28)	1651vs [b]				1413(0·39)
5	[a]		1657(1·06)	1578(0·19)	[a]	1484(0·26)	1421(0·15)
6	[a]		1633(1·07)	1575(0·36)	[a]	1484(0·45)	1420
7			1653(0·94)	1575(0·20)	1524(0·58)	1484(0·33)	1415(0·19)
8			1633(0·93)	1573(0·38)	1523(0·91)	1484(0·46)	1416(0·34)

No.	III amide	?	CH_3–N rock	Bands (cm.$^{-1}$) δC_{ar}–H		νC_{ar}–CO	
1	1276(0·32)	1163(0·12)	1150(0·08)	1071(0·05)	1030(0·04)	921(0·04)	
2	1275(0·35)	1215(0·22)	1150(0·10)	1071(0·05)	1033(0·05)	926(0·05)	
3							
4							
5	1282(0·37)	[a]	[1156(0·07)]	1072(0·07)	1036(0·07)	[a]	
6	1278(0·37)	[a]	[1154(0·07)]	1072(0·06)	1033(0·05)	[a]	
7							797(0·06)
8							797(0·07)

No.	Material				δC_{ar}–CO	γC_{ar}–H
9	Normal	Nujol	(mull)	Capillary [d]	935(0·78)	830(0·64)
10	89% ^{18}O	Nujol	(mull)	Capillary [d]	935(1·04)	826(0·68)

No.	γC_{ar}–H	γN–H		γC_{ar}–H [f]	γC_{ar}–H [f]
9	802(0·72)	716—706vs, br		696vs	685vs
10	800(0·79)	719vs	709vs 705vs	698vs	690(0·90)

[a] Absorption in this region is obliterated by the solvent band. [b] The high cell-thickness masks the absorption in the 1630—1460 cm.$^{-1}$ zone and below 1300 cm.$^{-1}$. [c] Measured only in the 1680—1410 and 880—710 cm.$^{-1}$ regions. [d] Measured only in the 940—670 cm.$^{-1}$ range. [g] This heading refers to the bands at 3050 cm.$^{-1}$ only, since the 3070—3080 bands contain a bonded N–H absorption (ref. 2, p. 205). [f] Ref. 2, p. 65. [g] *Ibid.*, p. 16.

Values in square brackets were observed with higher concentrations; their optical densities are, however, reduced in accord with the given concentration.

Methylbenzamide shows a higher tendency to form dimers than does ethylacetamide,[3] a 0·04M-solution of which in carbon tetrachloride is mainly monomeric while a 0·05M-solution of methylbenzamide shows the monomeric frequency almost solely as a shoulder. This is noteworthy and might be connected with the higher conjugation of the C=O group in the former.

The 0·007 g./ml. chloroform solutions, which show only a 3460—3470 cm.$^{-1}$ band in

[4] Ref. 2, p. 207.

the N–H range, are however clearly monomeric. A phenomenon similar to the effect of chloroform on the dissociation of amide dimers has been observed for benzamide [1d] and other (secondary) amides [3] and is the result of strong (CH · · · OC) interaction between the chloroform and the amide dissolved in it. This interaction also exists between bromoform and dissolved amide, as is shown by the comparable values for the amide C=O stretching frequencies in chloroform and bromoform (in normal methylbenzamide, *e.g.*, 1657 and 1653 cm.$^{-1}$, respectively, as compared with 1673 cm.$^{-1}$ for a CCl_4 solution), hence the amide in solutions of 0·0077—0·0093 g. in 1 ml. of bromoform is also mostly monomeric. Thus, all the solution results reported in Table 1, except those for 0·007 g./ml. carbon tetrachloride solutions, refer to monomeric methylbenzamides.

When the normal dimeric spectrum (in CCl_4) is compared with the monomeric absorption (in CCl_4 and, where no such data exist, in $CHCl_3$) it is seen that outside the N–H region the differences are usually very small and the bands appear in almost the same place in both spectra. Hence the *trans*-dimerization affects the N–H bond strength much more than it affects the binding force of even the C=O group.

The big changes observed in the frequency of the 1675—1633 cm.$^{-1}$ band on exchange of ^{16}O for ^{18}O in the amide, and/or on change of the solvent from carbon tetrachloride to bromoform, show unequivocally that this band is mainly due to the stretching of the C=O group. Thus, the isotopic decrease of this band in carbon tetrachloride (and chloroform) amounts to 24 cm.$^{-1}$ (from 1675 to 1651) as compared with 31 cm.$^{-1}$ for di-isopropyl ketone,[5] 29 cm.$^{-1}$ for benzophenone,[1a] and 24 cm.$^{-1}$ for benzamide.[1d] This is in harmony with the calculations of Miyazawa, Shimanouchi and Mizushima [6] for the 1653 cm.$^{-1}$ band of *N*-methylacetamide, according to which this band is 80% CO stretching, and seems to show that Price and Fraser's view,[7] that the secondary amide I frequency has in fact an asymmetrical OCN stretching nature, is somewhat exaggerated.

The value of 1675 cm.$^{-1}$ for C=O stretching of the monomeric normal methylbenzamide (in CCl_4) compares favourably with that (1690 cm.$^{-1}$) reported [1d] for the corresponding benzamide frequency, since it is known that monoalkyl substitution decreases such a frequency by some 10 cm.$^{-1}$ because of electronic effects.[8] The lower frequency (about 1667 cm.$^{-1}$) observed for an analogous band of *solid* *N*-ethylbenzamide [9] is no doubt the result of strong hydrogen-bonding in the solid state which as a rule lowers the amidic C=O frequency.[10]

The decrease in the C=O frequencies of monomeric methylbenzamide on changing the solvent from carbon tetrachloride to chloroform is 18 cm.$^{-1}$ for both of the isotopic modifications although it was smaller and somewhat different for the isotopic species of benzamide [1d] (15 for the normal and 11 for the labelled). This seems to suggest a somewhat stronger chloroform–amide interaction with the more polar secondary amides.

The band observed in all the spectra at about 1575 cm.$^{-1}$ is probably due to an aromatic C=C stretching [11] while the other aromatic C=C absorption expected,[11] at about 1500 cm.$^{-1}$, is probably masked by the strong 1524 cm.$^{-1}$ band. The latter seems to be the strong [1d] II amide band which is shown by hydrogen-bonded *N*-methylacetamide [6] at 1567 cm.$^{-1}$ and by solid *N*-ethylbenzamide [9] at about 1570 cm.$^{-1}$, as it is well known that hydrogen-bonding increases the frequency of such bands.[2] According to Miyazawa *et al.*,[6] ~60% of this absorption, with methylacetamide, is due to N–H bending and 40% to C–N stretching. That *N*-methylbenz[^{18}O]amide shows this band almost at the same place (1523) supports such an assignment. The even higher intensity of this band for the dimers also favours this interpretation since in the dimers the free charges on the nitrogen atoms

[5] Karabatsos, *J. Org. Chem.*, 1960, **25**, 315.
[6] Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1958, **29**, 611.
[7] Price and Fraser, *Proc. Roy. Soc.*, 1953, *B*, **141**, 66.
[8] Richards and Thompson, *J.*, 1947, 1248.
[9] Lenormant, *Ann. Chim.* (*France*), 1950, **5**, 476.
[10] Ref. 2, p. 209.
[11] Ref. 2, p. 69.

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can be expected to rise as a result of the hydrogen-bonding; such a rise should increase the absorption intensity of those frequencies which concern these atoms.

The bands at about 1480 and 1420 cm.$^{-1}$ seem to be due to antisymmetric and symmetric bending of the *N*-methyl groups, respectively, which in C–CH_3 groups cause absorption at about [12] 1460 and 1380 cm.$^{-1}$. In the case of $CH_3 \cdot ND_2$ (gas) these bands probably appear [13] at about 1470 and 1430 cm.$^{-1}$, respectively, while the symmetric N–CH_3 band of (hydrogen-bonded) *N*-methylacetamide [6] is at 1413 cm.$^{-1}$.

The 1282—1278 cm.$^{-1}$ band of monomeric *N*-methylbenzamide corresponds to the 1299 cm.$^{-1}$ III amide band of (bonded) methylacetamide [6] which was calculated [6] to be due 40% to C–N stretching and 30% to N–H bending. The exchange of ^{16}O for ^{18}O shifts it, in this case, by 4 cm.$^{-1}$ only, and this agrees with such an interpretation as also does the fact that it is affected moderately by dissociation and/or change of solvent from carbon tetrachloride to chloroform (normal dimer in CCl_4 1276; normal monomer in $CHCl_3$ 1282). This is so since it is known that such variations of conditions affect [14] the N–H bending and C–N stretching [1d] of amides.

The 1150 cm.$^{-1}$ bands are analogous to the 1159 cm.$^{-1}$ band of *N*-methylacetamide which was assigned to the CH_3–N rocking.[6] The 1072 and 1036 cm.$^{-1}$ bands seem to be due to the monosubstituted benzene moiety.[15] The absorptions observed with a Nujol mull of the isotopic amides are more difficult to assign to specific modes of vibration since the materials are then in a strongly hydrogen-bonded structure where the lattice forces affect seriously and split the original vibrations. It appears, however, that the 935 cm.$^{-1}$ absorption can be correlated with the stretching of the C_{ar}–CO bond since it is shown at the same place by solid *N*-ethylbenzamide,[9] at about 925 cm.$^{-1}$ by acetophenone,[16] at 932 cm.$^{-1}$ by benzoyl chloride,[1e] at 934 cm.$^{-1}$ by methyl benzoate [1e] (unaffected by ^{18}O), at 940 cm.$^{-1}$ in benzophenone,[1a] at 923 cm.$^{-1}$ in benzaldehyde,[17] and near 900 cm.$^{-1}$ in many substituted benzaldehydes.[18] This band seems to shift to 921—926 cm.$^{-1}$ for dimer solutions.

The 830 and 802 cm.$^{-1}$ (normal) bands (in $CHBr_3$ only one band at 797) correspond to the out-of-plane aromatic C–H bending frequencies of solid benzamides [1d] observed at 790 and 771 cm.$^{-1}$. The bands observed at 719—705 cm.$^{-1}$ are probably due to associated secondary amides NH out-of-plane bending, which is shown by *N*-methylacetamide [6] and other secondary amides [19] at about 720 cm.$^{-1}$.

The Intensity of the Isotopic C=O *Bands.*—The optical-density measurements for the C=O bands of the isotopic *N*-methylbenzamides in solution are given in Table 2, together with the molecular extinction coefficients and relative integrated absorption intensities (obtained by multiplying these coefficients by the corresponding apparent half-widths; the last, in cm.$^{-1}$, are added in parentheses after the intensities).

Table 2 seems to show that, as could be suspected, the intensity of the monomeric *N*-methylbenzamide C=O absorption in carbon tetrachloride is (as in benzamide) appreciably higher for the ^{18}O-modification than for the normal one, the respective mean relative integrated absorption values being 10,900 ± 300 and 8900 ± 300 units. These values can be compared with those of 12,800 and 10,400 for benzamide.[1d] The small increase in half-width of the C=^{18}O band in CCl_4 observed here (from 33 to 35·5) is also analogous to the change observed there [1d] (from 20 to 22). This increase was also found for other C=^{18}O bands.[1b,e] The mean integrated absorption results for the chloroform solutions of the two *N*-methylbenzamides, 12,400 ± 400 and 11,900 ± 400 units, are practically

[12] Ref. 2, p. 21.
[13] Gray and Lord, *J. Chem. Phys.*, 1957, **26**, 690.
[14] Ref. 2, p. 219.
[15] Ref. 2, p. 82.
[16] National Research Council, National Bureau of Standards Infrared Spectral Catalogue, card no. 289.
[17] Documentation of Molecular Spectra Catalogue, curve no. 2410, Butterworths, London
[18] Pinchas, *Analyt. Chem.*, 1957, **29**, 335.
[19] Ref. 2, p. 205.

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TABLE 2. *Absorption intensity of the isotopic* N-*methylbenzamides:* C=O *bands.*

Material	Frequency (cm.$^{-1}$)	Solvent	Concn. (g./l.)	Thickness (mm.)	Optical density	Mol. extinction coeff. (l. mole^{-1} cm.$^{-1}$)	Rel. integrated absorption (l. mole^{-1} cm.$^{-2}$)
Normal monomer ...	1675	CCl_4	0·122	20	0·478	264 ± 12	8700 ± 400 (33)
Normal monomer ...	1675	CCl_4	0·194	20	0·787	274 ± 7	9000 ± 300
89% ^{18}O monomer...	1651	CCl_4	0·126	20	0·504 [a]	308 ± 7 [b]	10,900 ± 300 (35·5)
89% ^{18}O monomer...	1651	CCl_4	0·144	20	0·581 [a]	310 ± 14 [b]	11,000 ± 500
Normal dimer	1673	CCl_4	5·94	0·5	0·588	267 ± 7	11,200 ± 300 (42)
89% ^{18}O dimer	1649	CCl_4	6·9	0·5	0·498 [a]	222 ± 9 [b]	11,100 ± 300 (50)
Normal monomer ...	1657	$CHCl_3$	5·62	0·5	0·784	377 ± 10	12,400 ± 400 (33)
89% ^{18}O monomer...	1633	$CHCl_3$	5·3	0·5	0·576 [a]	334 ± 16 [b]	11,700 ± 500 (35)
89% ^{18}O monomer...	1633	$CHCl_3$	6·28	0·5	0·709 [a]	347 ± 9 [b]	12,100 ± 400

[a] Uncorrected for the absorption of the normal amide content. [b] Corrected for the lower effective concentration.

identical, in analogy with the situation in the case of benzamide [1d] (14,500 in both modifications).

It is noteworthy that the C=O absorption intensity of the dimers is also the same in both of the isotopic methylbenzamides although their band half-widths are in this case appreciably different.

Experimental.—N-*Methylbenz*[^{18}O]*amide.* [^{18}O]Benzoyl chloride [1c] (90 atom % of ^{18}O) was dissolved in dry dioxan with cooling (ice-bath). Methylamine, dried over potassium hydroxide, was bubbled through it in excess. After ½ hr. the methylamine hydrochloride was filtered off and washed with benzene. The benzene–dioxan solution was dried (Na_2SO_4), decolorised with charcoal, and evaporated until crystals began to appear. The crystals were redissolved by adding dioxan and reprecipitated by dry light petroleum. The solid, m. p. 77—79°, contained 88·5 atom % of oxygen-18.

N-*Methylbenz*[^{16}O]*amide.* This was prepared in an identical manner from normal benzoyl chloride.

The infrared spectra were measured with a Perkin–Elmer model 12 C spectrophotometer equipped with a sodium chloride prism as already described.[1c].

THE WEIZMANN INSTITUTE OF SCIENCE,
REHOVOTH, ISRAEL

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523. *The Reactions of Organic Phosphates. Part V.* The Hydrolysis of Triphenyl and Trimethyl Phosphates.*

By P. W. C. BARNARD, C. A. BUNTON, D. R. LLEWELLYN, C. A. VERNON, and V. A. WELCH.

In neutral or acidic solution trimethyl phosphate undergoes hydrolysis with carbon–oxygen bond fission, and acid-catalysis is not observed. The second-order reaction with hydroxide ions, on the other hand, proceeds with phosphorus–oxygen bond fission. Similarly triphenyl phosphate is hydrolysed with phosphorus–oxygen bond fission in alkaline solution. The latter reaction, which has a low activation energy (*ca.* 10 kcal. mole^{-1}), has been shown not to involve isotopic exchange at the phosphoryl oxygen atom.

SIMPLE trisubstituted phosphate esters are known to be relatively alkali-labile: [1-3] with the exception of an investigation of trimethyl phosphate by Hudson and Harper,[4] however,

* Part IV, *J.*, 1961, 1636.

[1] Cavalier, *Compt. rend.*, 1898, **127**, 60.
[2] Plimmer and Burch, *J.*, 1929, 279.
[3] Bailly and Gaumé, *Bull. Soc. chim. France*, 1936, **53**, 1396.
[4] Hudson and Harper, *J.*, 1958, 1356.

little kinetic work has been reported. Blumenthal and Herbert [5] found that alkaline hydrolysis of trimethyl phosphate proceeds with phosphorus–oxygen bond fission. Their result for hydrolysis in acid solution (*ca.* 70% carbon–oxygen bond fission) is less informative since (*a*) the use of hydrochloric acid introduced complexities due to the possible formation of methyl chloride,[6] (*b*) secondary hydrolysis of the product, dimethyl phosphate, occurred under the experimental conditions, and (*c*) the rôle of acid-catalysed processes was not elucidated.

In this paper the results are presented of a kinetic and isotopic study of the hydrolyses of trimethyl and triphenyl phosphates. Preliminary accounts of our work have already appeared.[7, 8]

Experimental

Materials.—A commercial sample of trimethyl phosphate was fractionated; it had b. p. 74·1—74·5°/10·5 mm., $n_D^{24.7}$ 1·3922 (Found: C, 25·1; H, 6·9; P, 22·3. Calc. for $C_3H_9O_4P$: C, 25·7; H, 6·5; P, 22·2%). Commercial triphenyl phosphate was recrystallised three times from ethanol and had m. p. 49°. Diphenyl hydrogen phosphate was prepared from phenol and phosphorus oxychloride and had m. p. 68°. Dioxan was purified as described by Vogel.[9]

Table 1. *Hydrolysis of trimethyl phosphate (TMP) in aqueous alkali.*

T	[NaOH], M	[TMP], M	10^3k_2	T	[NaOH], M	[TMP], M	10^3k_2
35·0°	0·334	0·242	0·330	65·5°	0·122	0·062	3·35
35·0	0·313	0·0645	0·338	69·3	0·143	0·086	4·78
35·0	0·164	0·0667	0·340	73·0	0·123	0·060	5·90
35·0	0·0770	0·0619	0·335	35·0 *	0·0210	0·0234	0·247
44·7	0·346	0·248	0·748				

* In dioxan–water (75 : 25 v/v).

Kinetic Measurements.—(1) *Trimethyl phosphate in alkaline solution.* The sealed-tube technique was used. The tubes were opened under excess of acid, and the resulting solutions titrated with standard base, Methyl Red–Methylene Blue being used as indicator. The reactions did not proceed beyond the removal of one methyl group. This is consistent with the known resistance of dimethyl phosphate to alkaline hydrolysis.[10,11] Good second-order rate coefficients were obtained in each run. The results are shown in Table 1; k_2 has the units l. mole^{-1} sec.$^{-1}$.

Variations in the concentrations of the substrate are without effect on k_2. Change of solvent to dioxan–water (3 : 1 v/v) produces a small decrease in rate. The Arrhenius parameters (E and A), calculated from the data over the range 35·0—73·0°, are 16·2 kcal. mole^{-1} and $10^{8\cdot1}$ l. mole^{-1} sec.$^{-1}$, respectively.

(2) *Trimethyl phosphate in neutral and acidic solutions.* The reactions were followed by titration with standard base, Methyl Red–Methylene Blue being used as indicator, of the dimethyl phosphate produced. Because dimethyl phosphate is also hydrolysed in acidic solution, theoretical infinity values corresponding to the removal of one methyl group were used in the calculation of first-order rate coefficients, and the reactions were followed only to *ca.* 20% of reaction. With 0·2M-perchloric acid at 100° the first-order rate coefficient for the hydrolysis of trimethyl phosphate measured in this way was found to be $0{\cdot}373 \times 10^{-4}$ sec.$^{-1}$. Under the same conditions the corresponding value for dimethyl phosphate [10] is $0{\cdot}393 \times 10^{-5}$ sec.$^{-1}$. Calculation shows that, over the first 20% of the hydrolysis of trimethyl phosphate, disturbance due to secondary hydrolysis of the product is negligible.

A different procedure was necessary for experiments in which a relatively large amount of perchloric acid was initially present. Aliquot portions, after removal from a thermostat-bath, were exactly neutralised with sodium hydroxide, and a known excess of standard sodium

[5] Blumenthal and Herbert, *Trans. Faraday Soc.*, 1945, **41**, 611.
[6] Cherbuliez and Leber, *Helv. Chim. Acta*, 1952, **35**, 2539.
[7] Barnard, Bunton, Llewellyn, Oldham, Silver, and Vernon, *Chem. and Ind.*, 1955, 760.
[8] Vernon, *Chem. Soc. Spec. Publ.*, 1957, No. 8, 17.
[9] Vogel, "Textbook of Practical Organic Chemistry," Longmans, Green and Co., London, 1948, p. 177.
[10] Bunton, Mhala, Oldham, and Vernon, *J.*, 1960, 3293.
[11] Kumamoto, Cox, and Westheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 4858.

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hydroxide was then added. Titration with standard acid, after heating until all the trimethyl phosphate had hydrolysed, enabled the concentration of trimethyl phosphate remaining in the original experiment at any time, t, to be calculated. The precision of the rate coefficients obtained by this procedure was *ca.* ±10%.

Table 2 summarises the results obtained.

TABLE 2. *The hydrolysis of trimethyl phosphate* (ca. 0·25M) *in neutral and acid solutions.*

T	$[HClO_4]$ (M)	10^5k	T	$[HClO_4]$ (M)	10^5k_1
44·7°	—	0·016	100·1°	—	3·65
65·5	—	0·158	100·1	0·10	3·83
73·0	—	0·330	100·1	0·20	4·05
80·0	—	0·658	100·1	3·0	4·33

The Arrhenius parameters (E and A) for the solvolytic reaction are 22·7 kcal. mole^{-1} and $10^{8\cdot9}$ l. mole^{-1} sec.$^{-1}$, respectively.

(3) *Triphenyl phosphate in alkaline solution.* The rate of reaction with alkali in aqueous dioxan was followed by estimation of the phenol produced, by using the reagent introduced by Folin and Ciocalteu.[12] The following details of a run with 0·00624M-triphenyl phosphate and 0·0182M-sodium hydroxide in dioxan–water (3 : 2 v/v) at 10·1°, are typical. Dioxan (17·6 ml.), 60% dioxan–water (10 ml.), and dioxan containing 4·181 g. of triphenyl phosphate per 100 ml. (5·03 ml.) were mixed in a flask, which was placed in a thermostat bath at 10·1° and allowed to come to thermal equilibrium. Carbonate-free sodium hydroxide solution (0·1228N; 15·0 ml.) at 10·1° was then added, and the mixture made up to 100 ml. with 60% dioxan–water at 10·1°. Aliquot portions (10 ml.) were removed at appropriate time intervals and pipetted into flasks containing 0·12M-perchloric acid (5 ml.). Water (50 ml.) and Folin's reagent (5 ml.) were added, in the order stated, and the volume was made up to 100-ml. with water. After 80 min. the solutions were centrifuged at 3000g for 20 min. to remove precipitated triphenyl phosphate. Colour intensities were then measured in a Spekker photoelectric absorptiometer, a red filter being used. The contents of phenol were then determined by reference to a standard curve.

t (min.)	0	1·33	2·41	4·00	5·33	7·33
Phenol (mg./sample)	0·179	0·222	0·258	0·303	0·335	0·394
10^2k_2, l. mole^{-1} sec.$^{-1}$	—	0·507	0·532	0·485	0·467	0·467

Diphenyl phosphate undergoes slow hydrolysis in alkaline solution but the rate is too small to interfere with this procedure.

A few rates were measured by a simple acid–base titration method (*e.g.*, as described for trimethyl phosphate). Since, in this case, both products (*i.e.*, phenol and diphenyl phosphate) are acidic, second-order rate coefficients were calculated from the equation,

$$k_2 = \frac{2{\cdot}303}{t(2a - b)} \log_{10} \frac{b(a - x)}{a(b - 2x)}$$

where a and b are the initial concentrations of sodium hydroxide and triphenyl phosphate, respectively. In dioxan–water (3 : 1 v/v) at 35·0°, the mean values of k_2 were 0·0253 and 0·0227 l. mole^{-1} sec.$^{-1}$ for the colorimetric and acid–base method, respectively. In 60% dioxan–water the mean values of 10^2k_2 (l. mole^{-1} sec.$^{-1}$) at 0°, 10·1°, 24·7°, and 35·0° were 0·235, 0·477, 1·06, and 2·32, respectively. Hence $E = 10{\cdot}2$ kcal. mole^{-1} and $A = 10^{4\cdot9}$ l. mole^{-1} sec.$^{-1}$.

The solvolytic reaction was too slow for accurate measurement. The mean value of the first-order rate coefficient (100·1°) was $6{\cdot}0 \pm 0{\cdot}1 \times 10^{-6}$ sec.$^{-1}$.

(4) *Isotope experiments.* The hydrolysis of trimethyl phosphate was carried out under a variety of conditions in water enriched in oxygen-18. The concentrations of trimethyl phosphate were usually in the range 1·5—2·5M and the volumes of solutions were so chosen that *ca.* 3 ml. of pure methanol were finally recovered. Methanol was isolated and isotopically analysed as previously described.[13] The results are shown in Table 3, where N_s and N_m are the atom-percentages excess abundance of oxygen-18 in the solvent and in the isolated methanol,

[12] Folin and Ciocalteu, *J. Biol. Chem.*, 1927, **73**, 627.
[13] Bunton, Llewellyn, Oldham, and Vernon, *J.*, 1958, 3574.

respectively, and Q_c the proportion of the reaction proceeding with carbon–oxygen bond fission. Q_c is given simply by N_m/N_s since, under all the relevant conditions, the oxygen exchange of methanol is negligibly slow.[13]

The results show that, within the experimental error, the reaction in alkaline solution proceeds entirely with phosphorus–oxygen bond fission. Similarly in initially neutral or acidic solutions the reaction proceeds entirely with carbon–oxygen bond fission. For the reason already given, no ambiguity is introduced into these results by secondary hydrolysis of dimethyl phosphate. The experiment in which an attempt was made to keep the solution exactly neutral by addition of sodium hydroxide gave a result indicating the occurrence of both kinds of bond fission. Since the reaction with hydroxide ions is so much faster than the solvolysis, this presumably arises from local concentrations of sodium hydroxide in the addition process and has no mechanistic significance.

TABLE 3. *Isotope results: hydrolysis of trimethyl phosphate.*

Conditions	N_s	N_m	Q_c
3·44M-NaOH, 35°, complete reaction	0·423	0·014	0·03
0·62M-NaOH, 35°, complete reaction	0·957	0·002, 0·035	0·00, 0·04
Neutral (to Methyl Red) by addition of NaOH, 100°, 25% reaction	0·911	0·540	0·59
1·0M-$HClO_4$, 100° 28% reaction	0·647	0·616	0·95
0·1M-$HClO_4$, 100°, 28% reaction	0·337	0·341	1·01
Initially neutral, 28% reaction	0·647	0·647, 0·642	1·00, 0·99

The position of bond fission in the reaction of triphenyl phosphate and hydroxide ions was also determined. A solution (250 ml.) of triphenyl phosphate (0·025M) and sodium hydroxide (0·1M) in 75% dioxan–water containing 0·65% excess abundance of oxygen-18 in the water, was placed in a thermostat-bath at 35°. Phenol was extracted, distilled at 3 mm., and then pyrolysed to carbon monoxide, which was analysed mass-spectrometrically. The result showed that the isolated phenol contained $-0{\cdot}00_3$% excess abundance of oxygen-18. The reaction proceeds, therefore, with phosphorus–oxygen bond fission.

Experiments designed to detect oxygen exchange at the phosphoryl oxygen were carried out on both triphenyl and trimethyl phosphate. The procedures used depended on the amount of enriched water available. The following details are illustrative; (*A*) A solution (250 ml.) of triphenyl phosphate (*ca.* 0·02M) and sodium hydroxide (*ca.* 0·025M) in dioxan–water (3 : 1 v/v), containing excess abundance (*ca.* 1·0%) of oxygen-18 in the water, was allowed to react at 25° for 3·5 min. (*ca.* 43% reaction). Addition of excess of 0·1M-hydrochloric acid stopped the reaction. The mixture was extracted several times with petroleum. The combined extracts were washed (water), dried, and evaporated. The resulting solid was dried *in vacuo* over phosphoric oxide, and then had m. p. and mixed m. p. 46·5—48°. (*B*) Water (0·5 ml.) containing a large excess abundance of oxygen-18 (*ca.* 30%) was slowly added to a mixture of dioxan (3 ml.) and sodium (0·2 g.). Triphenyl phosphate (1·3 g.) was then added and the mixture was shaken for 5 min. at 25°. The extraction and isolation of triphenyl phosphate were then carried out as above.

Two methods were used for the determination of the isotopic abundance of the unchanged triphenyl phosphate.

(1) The phosphate was heated with mercuric chloride for 3 hr. at 525° *in vacuo* (Rittenberg and Ponticorvo's method [14]). The carbon dioxide so obtained was contaminated with volatile impurities which interfered with the mass-spectrometric analysis. These impurities were removed by passing the gas through a column (2 ft.) packed with silicone oil on Celite and maintained at −80°. This method of decomposition should eliminate all four of the oxygen atoms of triphenyl phosphate, although some differentiation between the phosphoryl oxygen and the three ester oxygen atoms may occur.

(2) A known weight of triphenyl phosphate was heated with *o*-phenylenediamine hydrochloride in the presence of a known amount of carbon dioxide at 325° for 3 hr. (Dahn, Moll, and Menassé's method [15]). A control experiment with isotopically normal triphenyl phosphate and $C^{18}O_2$ showed that *ca.* 60% exchange occurred under the experimental conditions. The method is, therefore, satisfactory for the qualitative detection of isotopic labelling in the phosphoryl oxygen atom. The three ester oxygen atoms will not be affected by this procedure.[16]

[14] Rittenberg and Ponticorvo, *Int. J. Appl. Rad. Isot.*, 1956, **1**, 208.
[15] Dahn, Moll, and Menassé, *Helv. Chim. Acta*, 1959, **52**, 1226.

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Table 4 gives the results obtained: N_s and N_p refer to the excess abundance of oxygen-18 in the water and in the unchanged phosphate, respectively.

TABLE 4. *Isotopic composition of phosphates isolated from partial hydrolysis.*

Substrate	N_s (%)	N_p (%)	Analysis *
Triphenyl phosphate	1·44	$0{\cdot}01_2$	D
,, ...	1·33	$0{\cdot}00_5$	R
,, ...	33	$0{\cdot}01_5$	R
Trimethyl phosphate	1·44	0·01	R

* D, Dahn, Moll, and Menassé's method [15]; R, Rittenberg and Ponticorvo's method.[14]

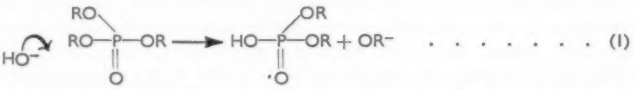
The small amount of enrichment actually observed probably arises from incomplete removal of impurities (*e.g.*, Me_2O, mass number 46). It is significant that the observed enrichment with triphenyl phosphate is no greater with water enriched by *ca.* 30% than with water enriched by *ca.* 1%. The isotope results indicate, therefore, that the hydrolytic reactions of triphenyl and trimethyl phosphate are not associated with appreciable isotopic exchange at the phosphoryl oxygen atoms.

The infrared spectrum of a solution (in carbon tetrachloride) of the triphenyl phosphate isolated from partial hydrolysis in the solvent containing heavily enriched water (33% excess abundance of oxygen-18) was compared, a Grubb-Parsons double-beam infrared spectrometer being used, with the spectrum of a solution (in carbon tetrachloride) of the initial material. The spectra were identical: in particular, the peaks of the doublet assigned to the P=O stretching [16] were at 1299 and 1314 cm.$^{-1}$ and 1301 and 1315 cm.$^{-1}$ for the initial and recovered samples, respectively. It is known [17] that the stretching frequency of the P=O group moves to lower frequencies (by *ca.* 30 cm.$^{-1}$) upon substitution of oxygen-16 for oxygen-18. Although this method is not sufficiently sensitive to detect a small isotopic enrichment, the result shows that no large isotopic exchange remains undetected by the other analytical methods.

DISCUSSION

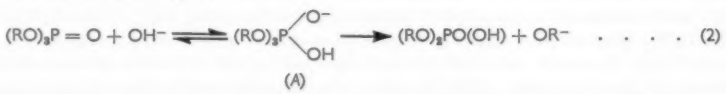
The reactions of trimethyl and triphenyl phosphate with hydroxide ions proceed with phosphorus–oxygen bond fission. The rates of the reactions are not much affected by solvent changes. For example, with trimethyl phosphate change of solvent from water to dioxan–water (3 : 1 v/v) reduces the rate by only *ca.* 25%. Triphenyl phosphate is, within the experimentally accessible range, the more reactive compound: at 35° in 75% dioxan–water, the rate factor is *ca.* 100. It would appear, therefore, that a correlation exists between rate and stability (as judged by the pK of the conjugate acid) of the displaced anion. However, in this case simple rate comparisons are ambiguous. Calculation shows that at 113·4°, the order of reactivity is reversed. It is probably better, therefore, to correlate the activation energy with the stability of the displaced anion.

These facts are consistent with the formulation of the reaction as a simple nucleophilic displacement (*i.e.*, of the S_N2 type) at the phosphorus atom:



(1)

However, for triphenyl phosphate the observed activation energy (10·2 kcal. mole^{-1}) is abnormally low for a reaction involving a negatively charged nucleophile and a neutral molecule. It seemed possible, therefore, that at least with triphenyl phosphate, hydrolysis involves an intermediate adduct (*A*):



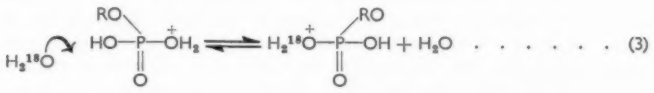
(2)

(*A*)

[16] Bellamy and Beecher, *J.*, 1952, 475.
[17] Holmann and Pinchas, *Bull. Res. Council Israel*, 1958, **7***A*, 101.

In the sequence (2), if the formation of (*A*) is relatively fast and reversible, and if all the steps are slower than proton transfers involving the OH and O^- groups of intermediate *A*, then hydrolysis will be associated with isotopic exchange at the phosphoryl oxygen atom. Experiments designed to test this were carried out both with triphenyl and trimethyl phosphate. No exchange at the phosphoryl oxygen atom has been detected with either compound. It appears, therefore, that the reactions of trisubstituted phosphates with hydroxide ion must be formulated as in scheme (1), *i.e.*, as S_N2 processes at a phosphorus centre.

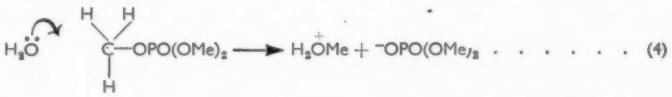
Holmann [18] has reported that the hydrolysis of di-isopropyl phosphorofluoridate is also not accompanied by isotope exchange at the phosphoryl oxygen atom. Oxygen-exchange reactions (although not necessarily involving the phosphoryl oxygen) have been observed only with phosphate mono- and di-esters in acid solution.[13,19] The evidence suggests, therefore, that quinquecovalent adducts of type (*A*) are never formed during the hydrolysis of phosphate esters, and that the exchange reactions observed in acid solution are simple S_N2 displacements of water by water, *i.e.*,



(3)

The results with triphenyl phosphate make it possible to compare the nucleophilic powers of water and hydroxide ions towards phosphorus.* The specific second-order rate coefficients at 100° in dioxan–water (3 : 2 v/v) are approximately 3×10^{-9} and 0·42 $sec.^{-1}$, respectively. Towards phosphorus, hydroxide ion is, therefore a better nucleophile than water by a factor of *ca.* 10^8. For attack on a saturated carbon atom the corresponding factor is much smaller, *i.e.*, *ca.* 10^4. Consequently, in a trisubstituted phosphate ester in which both carbon and phosphorus centres are open to substitution, hydroxide ion and water will tend to be selective for phosphorus and carbon, respectively.

Consistently with the above, trimethyl phosphate in the absence of hydroxide ions hydrolyses with carbon–oxygen bond fission. The reaction rate, in water, is not appreciably increased by the presence of up to 3M-perchloric acid; the reactive species is, therefore, the neutral molecule. The reaction presumably proceeds *via* an S_N2-type displacement on carbon, and analogous processes have been observed in methyl and dimethyl phosphate:[13,10]



(4)

The rates at 100° and in order of increasing methyl substitution are 0·5, 3·3, and 36·5 $\times 10^{-6}$ $sec.^{-1}$. After allowance for the statistical factor, the relative rates are 1·0, 3·3, and 24. The reaction is, therefore, favoured by increasing methyl substitution. The effect may, as discussed elsewhere,[8] be explicable in terms of the stability of the displaced anion.

Trimethyl phosphate shows no acid-catalysed hydrolysis in water as solvent. The rates of the acid-catalysed hydrolyses of methyl and dimethyl phosphate are approximately the same, *i.e.*, *ca.* 0·13 $\times 10^{-4}$ $sec.^{-1}$ at 100° with 3M-perchloric acid. If the rate for trimethyl phosphate has the same value, then the reaction would not be observed in water since it would be masked by the faster neutral reaction (*ca.* 0·4 $\times 10^{-4}$ $sec.^{-1}$ under the above conditions). Consistently, Thain [20] has shown that in dioxan–water (1 : 1 v/v),

* The solvolysis of triphenyl phosphate has not been shown to proceed with phosphorus–oxygen bond fission, but this can, for structural reasons, be assumed.

[18] Holmann, *Bull. Res. Council Israel*, 1958, **7***A*, 106.
[19] Cox, Wall, and Westheimer, *Chem. and Ind.*, 1959, 929.
[20] Thain, *J.*, 1957, 4694.

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in which the rate of the neutral reaction is much reduced, acid-catalysed hydrolysis of trimethyl phosphate may be observed.

We thank the Nuffield Foundation for a generous grant for apparatus.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1. [*Received, December 15th*, 1960.]

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524. *Conductimetric Titration of Sodium in Liquid Ammonia with Phosphine, Arsine, Stibine, and Germanes.*

By H. J. EMELÉUS and K. M. MACKAY.

The reaction of phosphine, arsine, stibine, and mono-, di-, and tri-germane with sodium in liquid ammonia has been studied by conductimetric titration, coupled with measurements of hydrogen evolution. A disodium derivative is formed by arsine and stibine in the early stages of the titration, though not by phosphine. The titration with monogermane resembles that with stannane, but the reaction with di- and tri-germane is more complex. Silylpotassium is formed when monosilane is added to potassium dissolved in diethylene glycol dimethyl ether.

CONDUCTIMETRIC titration of a solution of sodium in liquid ammonia with stannane, coupled with measurement of the hydrogen evolution, has shown that both stannylenedisodium, SnH_2Na_2, and stannylsodium, SnH_3Na, are formed in the early stages of the titration.[1] Towards its end, at low or zero sodium concentration, reaction (1) occurs, leading to the overall reaction (2):

$$SnH_2Na_2 + SnH_4 \longrightarrow 2SnH_3Na \quad \ldots \quad (1)$$

$$SnH_4 + Na \longrightarrow SnH_3Na + \tfrac{1}{2}H_2 \quad \ldots \quad (2)$$

This approach has now been used to study the reaction of sodium in liquid ammonia with phosphine, arsine, stibine, and mono-, di-, and tri-germane. Monosubstitution of hydrogen by an alkali metal is well established for phosphine, arsine, and monogermane and for some of their simpler organic derivatives. The only report of disubstitution by electropositive metals, however, is that of the preparation of solid compounds of the types PHM_2 and $AsHM_2$ (M = Li, Na, K, $\frac{1}{2}$Ca) in the thermal decomposition of phosphinyllithium, -sodium, -potassium, and -calcium and of arsinyl-lithium.[2] Solids with the approximate formula $AsHM_2$ have also been prepared by the action of arsine on films of lithium, sodium, or potassium.[3]

Addition of successive amounts of phosphine to a solution of sodium in liquid ammonia at −63·5° led to an almost linear fall in conductivity, as shown by the typical curve A in Fig. 1. There was a break at a phosphine : sodium ratio of unity and the conductivity remained constant when further phosphine was added. At this point the colour of the solution changed from deep blue to pale green. The results were reproducible. The hydrogen evolved on each addition of hydride was measured and for twenty-six observations, made in the course of three titrations, the mean hydrogen : phosphine ratio was 0·51, with a standard deviation of 0·027 (Fig. 2). These observations show the reaction to be: $Na + PH_3 \longrightarrow PH_2Na + \frac{1}{2}H_2$.

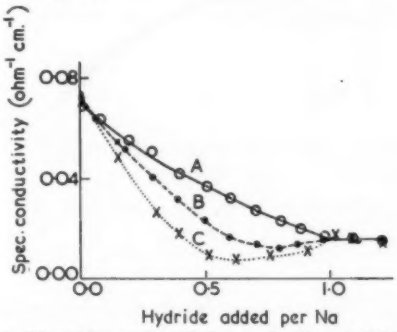
In a similar titration with arsine at −63·5°, a typical curve B for which is shown in Fig. 1, the conductivity fell more sharply as hydride was added and there was a shallow minimum at an arsine : sodium ratio of about 0·85. The colour was dark green at the

[1] Emeléus and Kettle, *J.*, 1958, 2444.
[2] Legoux, *Compt. rend.*, 1939, **209**, 47; *Bull. Soc. chim. France*, 1940, 545, 549.
[3] Jolly, *J. Amer. Chem. Soc.*, 1959, **81**, 1029.

minimum and changed sharply to clear yellow at an arsine : sodium ratio of unity. These results are similar to those for stannane,[1] and suggest that both AsH_2Na and $AsHNa_2$ were formed in the early stages of the titration and that, in its later stages, the reaction $AsHNa_2 + AsH_3 \longrightarrow 2AsH_2Na$ occurred. Various other mechanisms were considered but the foregoing seems the most probable and is supported by measurements of the hydrogen evolution (Fig. 2). In the early stages of the titration about 1·4 atoms of hydrogen were evolved for each molecule of arsine added, corresponding to a 40% formation of $AsHNa_2$. The hydrogen evolution fell off as the titration proceeded and was very slight towards the end. The overall reaction ratio was one atom of hydrogen per molecule of hydride. Arsine differs from stannane and germane (see below) in continuing to evolve hydrogen beyond the conductivity minimum, showing that some AsH_2Na was formed directly throughout.

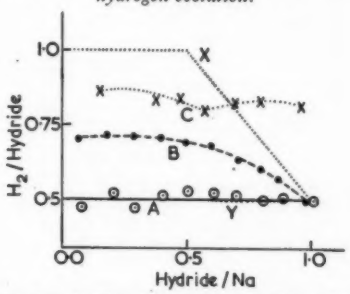
Results for stibine at −63·5° were less reproducible because of its lower stability, but they showed it to behave in a similar manner to arsine. Fig. 1 shows a steeper fall in conductivity and a minimum at a smaller hydride : sodium ratio than in the case of arsine,

FIG. 1. *The titration of the Group V hydrides: the variation in specific conductivity at −63·5°.*



A, *Phosphine against* 15·8 *mg. of sodium in* 2·30 *ml. of ammonia.* B, *Arsine against* 24·9 *mg. of sodium in* 3·29 *ml. of ammonia.* C, *Stibine against* 19·2 *mg. of sodium in* 2·89 *ml. of ammonia.*

FIG. 2. *The titration of the Group V hydrides : hydrogen evolution.*



A, B, C *as in Fig.* 1. X, Y, *evolution expected from complete formation of the disodium or monosodium derivative respectively.*

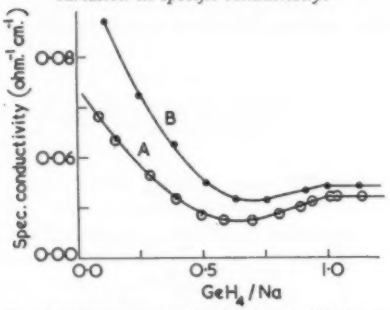
indicating a greater tendency to form the disodium derivative $SbHNa_2$. Evolution of hydrogen was also greater in the early stages though observations towards the end of the reaction were vitiated by decomposition, which led to deposition of a thin film of antimony on the reaction vessel above the liquid surface. The blue colour of the solution changed to dark green as the titration proceeded and this intense colour was discharged at a stibine : sodium ratio of approximately 1, leaving an orange solution. The essential data for the three hydrides are summarised here in a Table. These figures give the values for four runs with each hydride, except for the stibine values at the end point (*a*), which were taken from the two runs where decomposition was least.

	Molar ratio		
	Hydride : sodium		
Hydride	at min.	at end-point	Hydrogen : hydride
PH_3	—	0·98 ± 0·03	0·50 ± 0·01
AsH_3	0·83 ± 0·04	1·00 ± 0·03	0·49 ± 0·02
SbH_3	0·66 ± 0·05	1·02 (*a*)	0·53 (a)

The results for titrations with monogermane at −63·5° are shown in Fig. 3. The conductivity curve was similar to that for stannane, but the minimum was shallower and

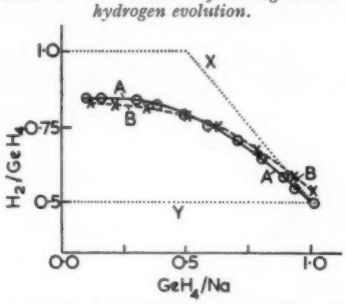
occurred at a higher hydride : sodium ratio. The blue colour was discharged at the minimum, leaving a pale yellow solution and a yellow-green precipitate. This precipitate dissolved almost completely on further additions of hydride up to a 1 : 1 ratio; it was not isolated, but was probably the disodium derivative. The hydrogen evolution in the monogermane titration is shown in Fig. 4. In the early stages approximately 1·6 atoms of hydrogen were evolved per molecule of hydride added. The overall molecular ratio of hydrogen to hydride was 0·52 and 90—95% of the total hydrogen had been evolved by the time the conductivity minimum was reached. These results support strongly the hypothesis that the disodium derivative is first formed in this case also. The slight excess of hydrogen probably arises from ammonolysis of the monogermane, which is known to occur but is much slower than that of monosilane (see below). The variation in the

FIG. 3. *The titration of monogermane: the variation in specific conductivity.*



A, *Monogermane against* 20·2 *mg. of sodium in* 3·66 *ml. of ammonia at* −63·5°. B, *Monogermane against* 19·0 *mg. of sodium in* 3·40 *ml. of ammonia at* −45°.

FIG. 4. *The titration of monogermane: hydrogen evolution.*



A *and* B, *as in Fig.* 3. X *and* Y, *as in Fig.* 2.

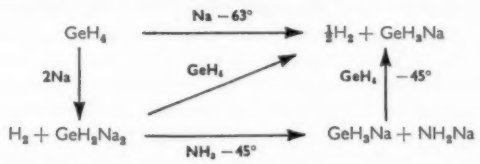
position of the minimum and of the end point in a series of experiments is shown in the Table.

Wt. of Na (mg.-atoms)	Concn. of Na solution (M)	GeH_4 : Na		Total H_2 : GeH_4
		At min.	At end-point	
0·684	0·175	0·72	1·04	0·53
0·908	0·246	0·80	0·99	0·53
0·893	0·241	0·69	1·02	0·51
0·878	0·238	0·71	0·98	0·52
0·844	0·238	0·70	1·08	0·53

In preliminary work on the effect of temperature on this reaction, observations were made at −45°. After an increment of hydride had been added at this temperature and thermal equilibrium had been reached, the conductivity became constant at one value (A) for 2—3 min. and then rose during about 3 min. to a higher value (B). An example of this was a rise in specific conductivity from 0·0804 (A) to 0·0966 ohm^{-1} $cm.^{-1}$ (B). This effect was reproducible and occurred in each titration until the free sodium had been used up. It was not observed at −63·5° and suggests that a second reaction occurred after the initial reaction of the hydride with the sodium solution.

A titration curve at −45°, plotted with the final conductivities, B, is shown in Fig. 3. The hydrogen evolution is shown on Fig. 4. Results at the two temperatures are very similar except that the minimum comes at a higher hydride : sodium ratio at the higher temperature. The same overall reaction appears to occur at the two temperatures, but the mechanism may be different. If it involved the solvent at the higher temperature, as shown, the rise in conductivity (A to B) could be interpreted as due to replacement of the

germylene dianion by the germyl anion and the more mobile solvent anion. Monogermane is known to react with sodamide in the manner indicated.[4]



It is relevant to the experiments with di- and tri-germane that Kraus and Carney,[5] in preparing monogermane by the acid-decomposition of magnesium germanide in liquid ammonia, removed higher hydrides from their product by treatment with a solution of sodium in ammonia. The products of this reaction were assumed to be GeH_3Na and GeH_2Na_2, formed by fission of the Ge–Ge bonds. They gave monogermane on treatment with an acid. The titration curve for digermane (Fig. 5) shows a sharp break at a reactant ratio of 0·5; at that point the colour of the solution also changed sharply from blue to pale green. This is the behaviour expected for the reaction $Ge_2H_6 + 2Na \longrightarrow 2GeH_3Na$ postulated by Kraus and Carney. However, hydrogen was evolved up to the 0·5 ratio in amounts proportional to the size of the hydride increment. The total amount

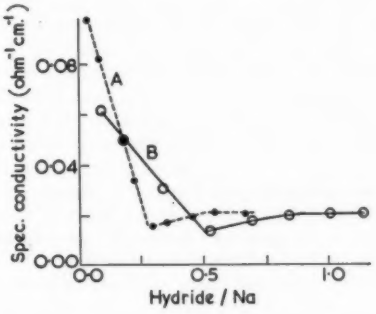


FIG. 5. *The titration of the higher germanes: the variation in the specific conductivity at* −63·5°.

A, *Digermane against* 15·1 *mg. of sodium in* 3·32 *ml. of ammonia.* B, 171 *mg. of trigermane against excess of sodium in* 2·97 *ml. of ammonia.*

was small and fell as the initial concentration of the sodium solution was increased. Thus, for a 1·82M-sodium solution a total of 0·18 atom of hydrogen per digermane molecule was obtained, while for 0·22M- and 0·12M-solutions the amounts were 0·22 and 0·46 atom, respectively. The position of the conductivity break was independent of the hydrogen evolved and this suggests that a second reaction, such as $Ge_2H_6 + 2Na \longrightarrow Ge_2H_4Na_2 + H_2$, occurs as well as that postulated by Kraus and Carney.

The curve for trigermane (Fig. 5) shows a minimum at a reactant ratio of 0·25, at which point the colour changed from blue to dark red. The conductivity rose between the 0·25 and the 0·5 ratios. The total hydrogen evolved in the titration, which was not carried to completion because of lack of material, was 0·201 mmole for 0·756 mmole of hydride. The ratio of hydrogen to hydride at the minimum was approximately 0·4, and at the 0·5 : 1 ratio had fallen to 0·3. This preliminary experiment shows that the reaction, which up to the minimum might be represented as $Ge_3H_8 + 4Na \longrightarrow 2GeH_3Na + GeH_2Na_2$, was in fact more complicated.

From these results for the various hydrides examined, the extent to which a disodium derivative is formed increases as the central atom becomes more electropositive. On this basis monosilane would show a minimal tendency to form a disodium derivative with the

[4] Glarum and Kraus, *J. Amer. Chem. Soc.*, 1950, **72**, 5399.
[5] Kraus and Carney, *J. Amer. Chem. Soc.*, 1934, **56**, 765.

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alkali metals. Addition of this hydride to a solution of sodium in ammonia led to a steady decrease in conductivity up to a hydride : sodium ratio of about 0·37. Beyond this point conductivity measurements were not reproducible and the hydrogen evolution increased considerably. The infrared spectrum of the solid left after removing ammonia showed no absorption at 2150 cm.$^{-1}$ (Si–H stretch frequency), but a strong band at 3300 cm.$^{-1}$ (N–H stretch), proving that complete solvolysis had occurred. To overcome this difficulty the reaction of monosilane with a solution of potassium in diethylene glycol dimethyl ether was examined. Addition of an excess of monosilane discharged the blue colour with evolution of hydrogen. Addition of methyl iodide to the product gave 1·42 mmoles of methylsilane from 1·46 mmoles of silane. This observation, which is being further studied, proves that silylpotassium can be formed when solvolysis does not occur, though it gives no indication of the rôle of silylenepotassium in the reaction.

Experimental

Phosphine, arsine, and monosilane were prepared by standard methods. Stibine was prepared by adding a slight excess of sodium borohydride rapidly to partially hydrolysed antimony trichloride in water at 20°. The hydride evolved was readily separated from water by distillation at −85° (yield 95%) in contrast to its difficult separation from ether when lithium aluminium hydride was used as a reducing agent (Found: *M*, 125. Calc. for H_3Sb: *M*, 125). The infrared spectrum was identical with that recorded in the literature.[6] The germanes were prepared by acid-hydrolysis of magnesium germanide;[7] the best yields (*ca.* 27%) were obtained with germanide prepared by heating stoicheiometric amounts of the finely powdered elements in hydrogen at 750—800° (24 hr.); the product was added fairly rapidly to 50% phosphoric acid at 50°; the hydrides GeH_4, Ge_2H_6, and Ge_3H_8 were obtained in the approximate ratio 9 : 4 : 1 and were separated by vacuum-fractionation and characterised by their molecular weights, vapour pressures, and infrared spectra (for GeH_4 and Ge_2H_6). The infrared spectrum of trigermane, which has not been recorded, showed strong absorption bands at 2080 and 801 cm.$^{-1}$ (with shoulders at 810 and 820 cm.$^{-1}$). The trigermane used was estimated, from its absorption spectrum, to contain about 4% of digermane.

The apparatus and technique used in the conductimetric titration were similar to those used in the experiments on stannane.[1] The amounts of hydride added in the titrations were measured manometrically in a bulb of known volume, by direct weighing, or by a combination of these methods, depending on the stability of the compound and its solubility in tap grease. Conductivities were measured at −63·5° in a bath of melting chloroform.

Reaction of Monosilane with Potassium in Diethylene Glycol Dimethyl Ether.—When an excess of monosilane was added to a solution of potassium in the ether of unknown concentration the blue colour was discharged. The unchanged hydride was separated and measured. It was found that 1·46 mmoles of monosilane yielded 0·718 mmole of hydrogen. An excess of methyl iodide was added to the solution. The volatile product was removed and separated from methyl iodide and solvent by distillation at −63·5°. It was methylsilane (1·42 mmoles) (Found: M, 43. Calc. for CH_6Si: *M*, 46); the identity was checked by the infrared spectrum.[8]

One of the authors (K. M. M.) thanks the Department of Scientific and Industrial Research for a Maintenance Grant.

University Chemical Laboratory,
Lensfield Road, Cambridge.

[*Received, January 19th*, 1961.]

[6] Smith, *J. Chem. Phys.*, 1951, **19**, 384.
[7] Dennis, Corey, and Moore, *J. Amer. Chem. Soc.*, 1924, **46**, 657.
[8] Kaye and Tannenbaum, *J. Org. Chem.*, 1953, **18**, 1751.

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525. α-1,4-*Glucosans. Part XII.*[1] *'End-group Assay of Glycogens by Oxidation with Sodium Metaperiodate.*

By D. J. Manners and A. Wright.

Four methods of end-group assay of glycogen by oxidation with sodium periodate have been critically compared. In three methods, varying degrees of overoxidation occurred, resulting in the production of additional formic acid. Determination of the initial amount of formic acid produced by the oxidation of 0·2% glycogen solution with 0·1M-sodium metaperiodate at room temperature (18—20°) gave values for the chain length in good agreement with those deduced by other methods of assay.

Although the end-group assay of glycogen by oxidation with sodium metaperiodate has been widely applied, the experimental conditions used by various workers differ considerably. Some examples are given in Table 1. We have therefore determined the maximum production of formic acid under different conditions from two glycogen samples whose average chain length ($\overline{CL}$) had previously been assayed by oxidation with potassium

Table 1. *Experimental conditions for the periodate oxidation of glycogen.*

Workers	Glycogen concn. (mg./ml.)	Periodate concn. (M)	Temp.	Duration of oxidn. (hr.)
Abdel-Akher and Smith [a]	0·4—2·0	0·05	5—6°	80
			0	180
Perlin [b]	2·0	0·1	16·6	*ca.* 30
Polglase, Smith, and Tyler [c]	10·0	0·16	2	*ca.* 72
Manners and Archibald [d]	4·0	0·032	2	*ca.* 240

[a] *J. Amer. Chem. Soc.*, 1951, **73**, 994. [b] *Ibid.*, 1954, **76**, 4101. [c] *J. Biol. Chem.*, 1952, **199**, 97. [d] *J.*, 1957, 2205.

Table 2. *Chain lengths of glycogens determined by oxidation with sodium metaperiodate under different conditions.*

Method	Time (hr.)	Apparent chain length (glucose residues) 49	96	168	216	260	336	696
Oyster glycogen *								
Abdel-Akher and Smith		—	—	—	10·1	9·3	8·6	7·8
Perlin		10·4	9·8	8·8	8·3	7·6	—	5·0
Polglase *et al.*		10·9	10·1	9·6	8·9	8·7	—	6·8
Manners and Archibald:	at 0°	14·9	12·8	11·9	11·3	10·5	—	10·0
	at *ca.* 17°	12·3	10·8	10·2	9·9	9·4	—	—
Rabbit liver glycogen †								
Abdel-Akher and Smith		—	—	—	12·9	11·6	10·3	8·5
Perlin		14·7	13·2	12·1	11·3	10·6	—	6·1
Polglase *et al.*		16·3	14·7	13·3	12·1	11·4	—	8·1
Manners and Archibald:	at 0°	21·6	18·2	16·9	16·4	16·0	—	14·0
	at 17°	18·4	16·7	15·6	15·0	14·7	—	12·5

* $\overline{CL}$ 10·4 by oxidation with potassium periodate.
† $\overline{CL}$ 13·9 by oxidation with potassium periodate.

metaperiodate.[2] This is a reliable and accurate method for the analysis of glycogens.[3] The results (Table 2) show that overoxidation (defined here as the production of formic acid in excess of that required by a Malaprade reaction) occurred in three of the experimental conditions, and that it was related to the temperature of the oxidation and the relative excess and concentration of oxidant. In all cases, an initial rapid production of formic acid was followed by a slower secondary reaction. The results in Table 2,

[1] Part XI, Archibald, Fleming, Liddle, Manners, Mercer, and Wright, *J.*, 1961, 1183.
[2] Bell and Manners, *J.*, 1952, 3641.
[3] Manners and Archibald, *J.*, 1957, 2205.

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and those obtained previously,[3] show that the rate of oxidation of different glycogens may differ; $\overline{CL}$ values cannot, therefore, be calculated with certainty from the production of formic acid after a particular period of oxidation.

Oxidation of glycogens by cold dilute solutions of sodium metaperiodate has been used extensively by F. Smith and his co-workers.[4] However, in our experiments (Tables 2 and 3) a very slow production of formic acid was noted after 180 hr. at 0° (cf. Table 1), so that there was some uncertainty about the final end-point. This may cause an error of 1—3 glucose residues for a 12-unit glycogen. In these estimations, the frequency of sampling is important; at short intervals of time the increase in production of formic acid may not exceed the experimental error involved in the titration with standard alkali, but at 48 or 72 hr. intervals a small increase may be detected. These conclusions are in agreement with recent studies by Professor R. Montgomery.[5]

TABLE 3. *Chain lengths of glycogens determined by oxidation with sodium metaperiodate in the conditions of Abdel-Akher and Smith.*

Glycogen sample	$\overline{CL}$ (KIO_4)	Time of oxidation (hr.):	Apparent chain length 216	288	360
Ascaris lumbricoides	12·0		13·5	10·8	9·4
Oyster	10·4		10·4	10·1	9·1
Rabbit liver VII	13·9		13·9	12·3	9·8

The conditions used by Polglase and his co-workers[6] were considered by them to give comparative rather than absolute values of $\overline{CL}$. Nevertheless, Warren and Whittaker[7] concluded that under these conditions oxidation was complete after 72 hr.; however, inspection of their results does not support this conclusion, and our results in Table 2 show clearly that formic acid production continues for several hundred hours. After oxidation for 72 hr., the apparent $\overline{CL}$ values of the oyster and rabbit-liver glycogen are 10·5 and 15·5, respectively (cf. values of 10·4 and 13·9 by oxidation with potassium periodate). The $\overline{CL}$ values obtained by Warren and Whittaker may therefore be too high by an amount varying from 0 to 2 glucose residues. This would account for the small but significant difference noted by them between the arithmetic mean of the $\overline{CL}$ values of some twenty glycogens as determined by periodate oxidation (12·9) and by enzymic assay of the same samples (12·4).

Under the conditions developed previously,[3] with a very limited excess of oxidant, no appreciable overoxidation occurs at 2° although the rate of oxidation is reduced to that found with potassium metaperiodate. The method gives reliable results: *e.g.*, human liver glycogen[8] and horse muscle glycogen[9] had $\overline{CL}$ values of 14·4 and 16·8, respectively (cf. values of 14·6 and 16·6 by the potassium method); it also enables the reduction of periodate to be analysed. The temperature of the oxidation is, however, critical and at room temperature (18—20°) slight overoxidation is apparent.

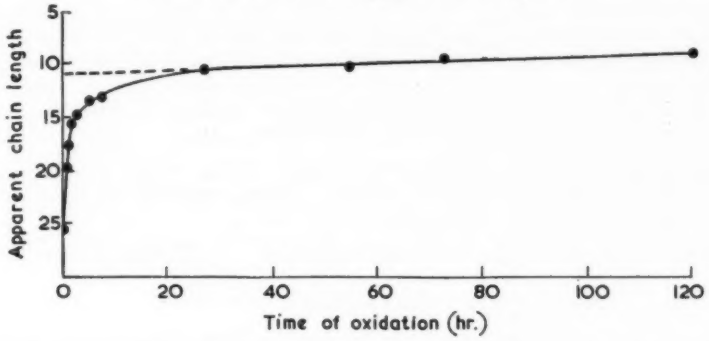
We conclude, in agreement with Peat, Turvey, and Evans,[10] that, provided experimental conditions are carefully controlled, oxidation by sodium metaperiodate provides an accurate method for the end-group assay of glycogens.

Alternative Method of Analysis.—When glycogen was oxidised under the conditions used by Perlin,[11] an approximately linear increase of production of formic acid with time occurred after 25 hr. (see Figure). In similar conditions, trehalose gave 2·2—2·3 mol.

[4] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 994.
[5] Montgomery, personal communication.
[6] Polglase, Smith, and Tyler, *J. Biol. Chem.*, 1952, **199**, 97.
[7] Warren and Whittaker, *Biochem. J.*, 1959, **72**, 288.
[8] Calderbank, Kent, Lorber, Manners, and Wright, *Biochem. J.*, 1960, **74**, 223.
[9] Lawrie, Manners, and Wright, *Biochem. J.*, 1959, **73**, 485.
[10] Peat, Turvey, and Evans, *J.*, 1959, 3341.
[11] Perlin, *J. Amer. Chem. Soc.*, 1954, **76**, 4101.

of formic acid (theor. 2·0 mol.). It was concluded that production of formic acid from the non-reducing end-group was complete within about 25 hr. and that the remaining acid arose from further oxidation of dialdehyde residues. It follows that extrapolation of the linear portion of the formic acid production *v.* time curve to zero time should provide

The rate of oxidation of oyster glycogen by sodium metaperiodate at 20°. The production of formic acid is shown as a decrease in apparent chain length.



an accurate measure of the formic acid arising solely from the non-reducing end-groups. This procedure has been applied to various polysaccharides, and the results (Table 4)

TABLE 4. *Chain lengths of polysaccharides determined by the extrapolation method.*

Sample	$\overline{CL}$ by extrapoln.	$\overline{CL}$ by KIO_4 oxidn.	Sample	$\overline{CL}$ by extrapoln.	$\overline{CL}$ by KIO_4 oxidn.
Human liver glycogen (A. K.)	14	15	Maize amylopectin	19	18 *
Human liver glycogen (S. K.)	6	6	Malt amylopectin	18 *	18 †
Oyster glycogen	11	10	Potato amylopectin	24	23
Rabbit liver VII glycogen ...	15	14	Potato amylopectin β-dextrin	10	9
Rabbit liver VIII glycogen ...	14	13			

* Determined by Mr. G. A. Mercer. † Kindly supplied by Dr. G. O. Aspinall (cf. Aspinall, Hirst, and McArthur, *J.*, 1955, 3075).

are in good agreement with those from assays of the same samples by oxidation with potassium metaperiodate. Within certain limits, the extrapolated $\overline{CL}$ value is independent of the relative concentration of oxidant and of temperature, although the rate of over-oxidation is temperature-dependent. The method requires an oxidation period only one-half that of the other procedures and, with suitable modification, should be applicable to the microanalysis of the small quantities of glycogen which are available in most clinical and metabolic studies.

EXPERIMENTAL

Analytical Methods.—The methods described previously [3] were used, solutions of polysaccharide samples being adjusted to pH 5·8 before oxidation.

Comparison of Oxidation Conditions.—Glycogen samples (100 or 250 mg.) were oxidised under the conditions described in Table 1, the final volumes of the mixtures being increased proportionally. The results are shown in Table 2. Further samples of glycogen (100 mg.) were oxidised by the method of Abdel-Akher and Smith; [4] see Table 3 for results.

Overoxidation of Glycogen.—Oyster glycogen (200 mg.) was oxidised by Perlin's method [11] at 20°, the total volume being 100 ml. Samples (5 or 10 ml.) were removed at intervals; the results are shown in the Figure.

Human liver glycogen [8] (100 mg.) was then oxidised under three different conditions: (*a*) by Perlin's method [11] at 20°; (*b*) as (*a*) but with twice the concentration of periodate; (*c*)

Time of oxidn. (hr.)	Apparent $\overline{CL}$ values (*a*)	(*b*)	(*c*)	Time of oxidn. (hr.)	Apparent $\overline{CL}$ values (*a*)	(*b*)	(*c*)
24	—	—	11·1	95	12·0	11·8	4·1
49	12·9	13·0	8·4	140	11·0	11·0	—
75	—	—	5·5	180	10·7	10·6	—

as (*a*) but at 37°. In each experiment, a graph of formic acid production against time was prepared, and by extrapolation to zero time, a $\overline{CL}$ value obtained, namely, (*a*) 13·9, (*b*) 13·9, (*c*) 13·8 glucose residues.

Several samples of glycogen (70—100 mg.) and amylopectin (*ca.* 200 mg.) were oxidised by Perlin's method at 20° and $\overline{CL}$ values obtained by extrapolation as above. The results are given in Table 4.

Trehalose (10—20 mg.) was also oxidised under these conditions: after 26 hr., 2·1 mol. of formic acid were released, and after 94 hr., 2·2—2·3 mol.

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Department of Chemistry, University of Edinburgh. [*Received, January 30th*, 1961.]

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526. *Reactions with Asymmetric Diarylethylenes. Part VI.* Reduction of 2-Bromo-1,1-di-p-alkoxyphenylethylenes by Thiophenols, and Addition of These Thiols to 1,1-Di-p-alkoxyphenylethylenes.*

By Wadie Tadros and Gamil Aziz.

1,1-Di-*p*-alkoxyphenyl-2-bromoethylenes are reduced by thiophenols to products whose nature depends on the substituents present in the thiophenols.

Thiophenols add to 1,1-di-*p*-alkoxyphenylethylenes in a reaction catalysed by hydrogen bromide. The stability of the products depends on the substituent in the thiophenol.

Reaction between anthrone and 1,1-di-*p*-alkoxyphenyl-2-bromoethylenes gives a number of compounds including dianthronyl, the 1,1-di-*p*-alkoxyphenylethylene, and the 1,1,4,4-tetra-*p*-alkoxyphenylbuta-1,3-diene.[1] When anthrone was replaced by thiophenol, the bromo-compound was reduced to the 1,1-dialkoxyethylene but the nature of the products was influenced by the relative quantities of the reactants. With 2 mol. of thiophenol, the main products were the ethylene, diphenyl disulphide, and hydrogen bromide:

$$(p\text{-RO}\cdot C_6H_4)_2\cdot C{:}CHBr + 2PhSH \longrightarrow (p\text{-RO}\cdot C_6H_4)_2\cdot C{:}CH_2 + HBr + Ph_2S_2$$

With one mol., the main product was 1,1,4,4-tetra-*p*-alkoxyphenylbuta-1,3-diene; only 0·5 mol. of the bromoethylene was reduced to the ethylene, $Ar_2C{:}CH_2$, leaving the other 0·5 mol. to react with this ethylene to give the butadiene according to the mechanism reported earlier.[1]

On extending the work to substituted thiophenols, it was found that the reaction was influenced by both the nature and the position of the substituent. With 2 mol. of toluene-*m*-thiol, the reaction proceeded as shown above. On the other hand, on boiling a solution of 2-bromo-1,1-di-*p*-methoxyphenylethylene and toluene-*p*-thiol in acetic acid, small quantities of 1,1,4,4-tetra-*p*-methoxyphenylbuta-1,3-diene and 4,4′-dimethoxystilbene were obtained under these conditions. Further study is being carried out to throw light

* Part V, *J.*, 1958, 4210.

[1] Tadros and Sakla, *J.*, 1957, 3210.

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on the formation of the stilbene. It may be mentioned, however, that 4,4'-dimethoxystilbene was formed from 2-bromo-1,1-di-*p*-methoxyphenylethane [2] in boiling acetic acid. The same stilbene was readily obtained from the bromoethane in boiling ethylene glycol in the presence or absence of silver acetate. *p*-Nitrobenzenethiol and 2-bromo-1,1-di-*p*-methoxyphenylethylene gave 1,1-di-*p*-methoxyphenyl-1-*p*-nitrophenylthioethane, both reduction and addition occurring. This thio-compound was readily obtained by interaction between *p*-nitrobenzenethiol and 1,1-di-*p*-methoxyphenylethylene.

The addition took place also with other thiophenols and was found to be catalysed by hydrogen bromide. Whereas the nitroarylthioethane was stable, 1,1-di-*p*-methoxy(or ethoxy)phenyl-1-phenylthioethane was unstable, darkening on storage; when treated with a mixture of hydrochloric and acetic acid or with alcoholic potassium hydroxide, it partly regenerated the ethylene. 1,1-Di-*p*-methoxyphenyl-1-*p*-tolylthioethane was more stable than the 1-phenylthioethane, but less so than the nitro-compound.

An attempt to condense 2-bromo-1,1-di-*p*-methoxyphenylethane with thiophenol or *p*-nitrobenzenethiol was unsuccessful. A small quantity of 4,4'-dimethoxystilbene was formed in acetic acid; 1,1-di-*p*-methoxyphenylethylene was obtained on treating the 2-bromoethane with sodium thiophenoxide in alcohol.

Experimental

Reactions between 1,1-*Di*-p-*alkoxyphenyl*-2-*bromoethylenes and Thiophenols.*—(a) *Reactions with thiophenol in boiling acetic acid.* (i) This is exemplified by the following: A solution of 2-bromo-1,1-di-*p*-methoxyphenylethylene (3·19 g.) and thiophenol (2·2 g.) in acetic acid (50 c.c.) was refluxed for 1 min. The solution, which became olive-green, was diluted with cold water, and the product was extracted with ether. The ethereal solution was washed with water, 5% aqueous sodium hydroxide, and again water. Ether was distilled off and the residue recrystallised from alcohol from which colourless 1,1-di-*p*-methoxyphenylethylene (1·1 g.) separated, having m. p. and mixed m. p. with an authentic sample [3] 140—142°. The alcoholic mother-liquor, on storage, gave diphenyl disulphide (0·8 g.), which on recrystallisation from alcohol had m. p. 59—60° alone or mixed with an authentic sample.[4] (ii) A solution of 2-bromo-1,1-di-*p*-ethoxyphenylethylene (2 g.) and thiophenol (1·27 g.) in acetic acid (30 c.c.) gave 1,1-di-*p*-ethoxyphenylethylene (0·6 g.), m. p. and mixed m. p. with an authentic sample [5] 142°, and diphenyl disulphide (0·22 g.). (iii) A solution of 2-bromo-1,1-di-*p*-butoxyphenylethylene (2 g.) and thiophenol (1·08 g.) in acetic acid (30 c.c.) gave 1,1-di-*p*-butoxyphenylethylene (0·6 g.), m. p. and mixed m. p. with an authentic sample [1] 125°, and diphenyl disulphide (0·3 g.).

(b) *Reaction at room temperature.* A mixture of the bromomethoxy-compound (0·64 g.) and thiophenol (0·22 g.) in acetic acid (10 c.c.) was left at room temperature for 10 days. The solution acquired an olive-green colour and a precipitate was gradually formed. On recrystallisation, this precipitate gave 1,1,4,4-tetra-*p*-methoxyphenylbuta-1,3-diene [6] (0·15 g.), m. p. and mixed m. p. 206—207°.

(c) *Reaction between* 2-*bromo*-1,1-*di*-p-*methoxyphenylethylene and toluene*-m-*thiol.* Repetition of experiment (a, i) with 2-bromo-1,1-di-*p*-methoxyphenylethylene (1 g.) and toluene-*m*-thiol (0·78 g.) in acetic acid (20 c.c.) gave 1,1-di-*p*-methoxyphenylethylene (0·35 g.) and di-*m*-tolyl disulphide,[7] an oil.

(d) *Reaction between* 2-*bromo*-1,1-*di*-p-*methoxyphenylethylene and toluene*-p-*thiol.* A solution of the bromo-compound (1 g.) and toluene-*p*-thiol (0·78 g.) in acetic acid (15 c.c.) was refluxed for 3 min. The green solution was diluted with cold water and extracted with ether, and the ethereal solution was washed with alkali and water. Ether was distilled off and the residue recrystallised from alcohol from which 4,4'-dimethoxystilbene (0·049 g.) separated, having m. p. and mixed m. p. with an authentic sample [8] 210°. The alcoholic mother-liquor gave, on

[2] Harris and Frankforter, *J. Amer. Chem. Soc.*, 1926, **48**, 3144.
[3] Pfeiffer and Wizinger, *Annalen*, 1928, **461**, 144.
[4] Vogt, *Annalen*, 1861, **119**, 142.
[5] Tadros and Aziz, *J.*, 1951, 2553.
[6] Bergmann, Szmuszkowicz, and Diamant, *J. Amer. Chem. Soc.*, 1949, **71**, 2968.
[7] Hübner and Post, *Annalen*, 1873, **169**, 1.
[8] Tadros and Ekladius, *Nature*, 1950, **166**, 525; Tadros, Ekladius, and Sakla, *J.*, 1954, 2351.

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storage, 1,1,4,4-tetra-*p*-methoxyphenylbuta-1,3-diene (0·02 g.), m. p. and mixed m. p. 204—205°. The bromo-compound was partly recovered together with other products; the reaction is being studied in more detail.

(e) *Reaction between* 2-*bromo*-1,1-*di*-p-*methoxyphenylethylene and* p-*nitrobenzenethiol.* A mixture of the bromo-compound (1 g.) and *p*-nitrobenzenethiol (0·48 g.) in acetic acid (30 c.c.) was left overnight at room temperature. The solution became olive-green and a precipitate was formed. This precipitate was filtered off and recrystallised from acetic acid, from which yellow di-*p*-nitrophenyl disulphide (0·15 g.) separated, having m. p. and mixed m. p. with an authentic sample [9] 180—181°. The main olive-green mother-liquor was diluted with water and extracted with ether. The ethereal solution was washed with water and alkali, and the ether was distilled off. The residue, recrystallised from alcohol, gave yellow 1,1-*di*-p-*methoxyphenyl*-1-p-*nitrophenylthioethane* (0·22 g.), m. p. 135° (Found: C, 67·2; H, 5·6; N, 3·3; S, 8·2. $C_{22}H_{21}NO_4S$ requires C, 66·8; H, 5·3; N, 3·5; S, 8·1%).

Addition of Thiophenols to 1,1-*Di*-p-*methoxy(or ethoxy)phenylethylene.*—(a) (i) A mixture of 1,1-di-*p*-methoxyphenylethylene (1 g.) and thiophenol (0·45 g.) in acetic acid containing hydrogen bromide (25 c.c. to which was added 0·3 c.c. of acid saturated with hydrogen bromide) was refluxed for 3 min. The olive-green solution was diluted with cold water and extracted with ether. The ethereal solution was washed with alkali and water and evaporated. The residue, recrystallised from methyl alcohol, gave colourless 1,1-*di*-p-*methoxyphenyl*-1-*phenylthioethane* (0·3 g.), m. p. 75—76° (Found: C, 75·0; H, 6·3; S, 9·4. $C_{22}H_{22}O_2S$ requires C, 75·4; H, 6·3; S, 9·1%). (ii) The corresponding diethoxyethylene (1 g.) and thiophenol (0·41 g.) gave colourless 1,1-*di*-p-*ethoxyphenyl*-1-*phenylthioethane* (0·3 g.), m. p. 115° (Found: C, 76·0; H, 5·5; S, 8·6. $C_{24}H_{26}O_2S$ requires C, 76·2; H, 6·9; S, 8·5%).

(b) *Addition of toluene*-p-*thiol to the dimethoxyethylene.* By reaction as in section (a, i), toluene-*p*-thiol (0·51 g.) gave colourless 1,1-*di*-p-*methoxyphenyl*-1-p-*methylphenylthioethane* (0·25 g.), m. p. 65° (Found: C, 75·8; H, 6·9; S, 8·7. $C_{23}H_{24}O_2S$ requires C, 75·8; H, 6·6; S, 8·8%). In the absence of hydrogen bromide, neither the thiophenol nor the toluene-*p*-thiol added to the ethylene.

(c) *Addition of* p-*nitrobenzenethiol to the dimethoxyphenylethylene.* A mixture of the ethylene (1 g.) and *p*-nitrobenzenethiol (0·63 g.) in acetic acid containing hydrogen bromide (50 c.c. to which was added 0·6 c.c. of acid saturated with hydrogen bromide) was refluxed for 3 min., then left to cool. Di-*p*-nitrophenyl disulphide (0·2 g.), m. p. and mixed m. p. 181°, separated first. The mother-liquor was diluted with water, the product was extracted with ether, and the ethereal solution was washed with alkali and water. Ether was distilled off and the residue recrystallised from alcohol, from which 1,1-di-*p*-methoxyphenyl-1-*p*-nitrophenylthioethane separated as yellow crystals (0·25 g.) showing no depression in the m. p. (135°) on admixture with an authentic sample. In the absence of the hydrogen bromide, the nitrothioethane was obtained but it required a longer time (30 min.) to obtain the same yield.

Effect of Acid and Alkali on 1,1-*Di*-p-*methoxyphenyl*-1-*phenylthioethane.*—(*a*) A solution of the sulphur compound (0·2 g.) in acetic (10 c.c.) and concentrated hydrochloric (1 c.c.) acid was refluxed for 30 min. The olive-green solution deposited, on cooling, 1,1-di-*p*-methoxyphenylethylene (0·05 g.), m. p. and mixed m. p. 141—142°.

(*b*) A mixture of the sulphur compound (0·25 g.) and potassium hydroxide (0·3 g.) in alcohol (25 c.c.) was refluxed on the water-bath for 2 hr. On cooling, the dimethoxyethylene (0·05 g.) separated as colourless crystals, m. p. and mixed m. p. 142°.

Attempt to Condense 2-*Bromo*-1,1-*di*-p-*methoxyphenylethane with Thiophenol.*—(*a*) A solution of the 2-bromoethane (2 g.) and thiophenol (0·68 g.) in acetic acid (40 c.c.) was refluxed for 3 min. On cooling, colourless 4,4′-dimethoxystilbene (0·21 g.), m. p. and mixed m. p. 209—210°, separated. No condensation product could be obtained.

(*b*) A mixture of the 2-bromoethane (2 g.) and thiophenol (0·68 g.) in alcoholic sodium ethoxide (0·143 g. of sodium dissolved in 60 c.c. of alcohol) was refluxed for 1 hr. The alcoholic solution was concentrated, diluted with water, and extracted with ether. Ether was distilled off and the residue, recrystallised from alcohol, gave dimethoxyethylene, having m. p. and mixed m. p. 141—142°.

(*c*) The preceding experiment but with the 2-bromo-ethoxy-ethane gave no condensation product and the ethoxy-ethylene, m. p. and mixed m. p. 142°, was formed.

[9] Wohlfahrt, *J. prakt. Chem.*, 1902, **66**, 551.

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Conversion of 2-Bromo-1,1-di-p-methoxyphenylethane into 4,4'-Dimethoxystilbene.—(*a*) A solution of the 2-bromoethane (1 g.) in acetic acid (20 c.c.) was refluxed for 3 min. On cooling, 4,4'-dimethoxystilbene (0·1 g.), m. p. and mixed m. p. 210°, was obtained. Prolonging the time of boiling increased the yield of stilbene (0·19 g. after 30 min.; 0·23 g. after 90 min.). The reaction is being studied in more detail.

(*b*) A solution of the 2-bromoethane (0·5 g.) in ethylene glycol (15 c.c.) was refluxed for 30 min. On cooling, 4,4'-dimethoxystilbene (0·15 g.), m. p. and mixed m. p. 209°, was obtained.

(*c*) The preceding experiment but with silver acetate (0·52 g.) and 2-bromoethane (1 g.) in ethylene glycol (30 c.c.) gave a product (0·2 g.), m. p. 188°. This gave, on recrystallisation from acetic acid, the dimethoxystilbene (0·15 g.), m. p. and mixed m. p. 210°.

DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, CAIRO UNIVERSITY, EGYPT, U.A.R. [*Received, October 6th*, 1960.]

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527. *Reactions with Asymmetric Diarylethylenes. Part VII.* A New Synthetic Route to Tetra-arylallenes.*

By WADIE TADROS, ALFY BADIE SAKLA, and ABDUL AZIZ AMIN HELMY.

Diphenylmethyl chloride or bromide added readily to asymmetric diarylethylenes, giving tetra-arylpropenes. With bromine these afforded tetra-aryl-2-bromopropenes whose structure was confirmed by ozonolysis and which with alcoholic potassium hydrioxide afforded tetra-arylallenes.

Triphenylmethyl chloride also added to the asymmetric diarylethylenes, giving penta-arylpropenes.

WE report a new synthetic route to tetra-arylallenes. Diphenylmethyl chloride or bromide added to asymmetric diarylethylenes, to give a product which underwent dehydrohalogenation readily with the formation of tetra-arylpropenes (I). These propenes were also obtained on passing hydrogen chloride or hydrogen bromide through a benzene solution of diphenylmethanol and the ethylene,[3] diphenylmethyl chloride or bromide being apparently formed before initiation of the reaction. Triphenylmethyl chloride also added to the ethylenes, giving the penta-aryl propenes. The simplest member of the series, tetraphenylpropene (I; R = H) was obtained earlier by Vorländer and Siebert [1a] and by Straus and Ehrenstein.[2]

Treating the tetra-arylpropenes with bromine gave bromo-compounds (II) whose structure was confirmed by ozonolysis; and the bromo-compounds with alcoholic potassium hydroxide gave the tetra-arylallenes (III). These reactions were effected by starting from 1,1-diphenylethylene and its di-*p*-methoxy-, -ethoxy-, -propoxy-, and -isopropoxy-derivatives. Tetraphenylallene itself has been obtained previously [1a,3] but three of the four derivatives which we prepared are new.

$$Ar_2C{:}CH_2 + Ph_2CHX \longrightarrow [Ar_2CX{\cdot}CH_2{\cdot}CHPh_2] \longrightarrow Ar_2C{:}CH{\cdot}CHPh_2\ (I) \longrightarrow$$

$$[Ar_2CBr{\cdot}CHBr{\cdot}CHPh_2] \longrightarrow \underset{(II)}{Ar_2C{:}CBr{\cdot}CHPh_2} \longrightarrow \underset{(III)}{Ar_2C{:}C{:}CPh_2}$$

In an attempt to add diphenylmethyl bromide to 2-bromo-1,1-diphenylethylene the latter was recovered unchanged and diphenylmethyl ethyl ether was formed on treating the reaction mixture with ethyl alcohol.

In tests on groups of 5 ovariectomised mice (average wt., 25 g.), tetraphenylallene and

* Part VI, preceding paper.

[1] (*a*) Vorländer and Siebert, *Ber.*, 1906, **39**, 1024; (*b*) Vorländer and Weinstein, *Ber.*, 1923, **56**, 1122.

[2] Straus and Ehrenstein, *Annalen*, 1925, **442**, 93.

[3] Staudinger and Meyer, *Helv. Chim. Acta*, 1922, **5**, 656; Vorländer, Osterburg, and Meyer, *Ber.*, 1923, **56**, 1136; Ziegler and Ochs, *Ber.*, 1922, **55**, 2257; Maitland and Mills, *J.*, 1936, 987; Ziegler, *Annalen*, 1923, **434**, 34; Bergmann, Hoffmann, and Meyer, *J. prakt. Chem.*, 1932, **135**, 245.

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1,1-di-*p*-methoxyphenyl-3,3-diphenylprop-1-ene and its 2-bromo-derivative (5 mg. in 0·4 c.c. of olive oil, injected subcutaneously during 2 days) showed practically no activity.

Experimental

1,1,3,3-*Tetra-arylpropenes*.—This is exemplified by the preparation of tetraphenylpropene. (*a*) A solution of diphenylmethyl bromide (2·47 g., 0·01 mole) or chloride (2·02 g.), and 1,1-diphenylethylene (1·8 g., 0·01 mole) in dry benzene (30 c.c.) was refluxed on the water-bath for 6 hr., becoming yellow and then green with evolution of halogen acid. Benzene was distilled, and the residue was digested for 30 min. with potassium hydroxide (1 g.) in alcohol (30 c.c.). The mixture was cooled, diluted with water (50 c.c.), and extracted with ether and the extract was washed with water. The ether was distilled off and the residue recrystallised from alcohol from which 1,1,3,3-tetraphenylpropene [1a] (2·1 g.) separated as colourless crystals, m. p. 127° (Found: C, 93·5; H, 6·4. Calc. for $C_{27}H_{22}$: C, 93·6; H, 6·4%). The treatment with alkali was merely precautionary because, as just indicated, the intermediate lost halogen acid spontaneously in the hot reaction mixture.

(*b*) Experiment (*a*) was repeated without use of a solvent, the mixture being heated in a boiling-water bath for 6 hr. and the product treated with alcoholic potassium hydroxide as above. 1,1,3,3-Tetraphenylpropene (2 g.) (from alcohol) had m. p. and mixed m. p. 127°.

(*c*) Hydrogen chloride or bromide gas was passed for 1 hr. through a boiling solution of diphenylmethanol (1·84 g., 0·01 mole) and 1,1-diphenylethylene (1·8 g., 0·01 mole) in dry benzene, then boiling was continued for further 5 hr., the same changes in colour as in (*a*) occurring; 1,1,3,3-tetraphenylpropene (2·1 g.) was obtained.

The following propenes similarly prepared; they crystallised from alcohol in 60—65% yield). 1,1-*Di*-p-*methoxyphenyl*-3,3-*diphenylprop*-1-*ene*, m. p. 86—88° (Found: C, 85·8; H, 6·6. $C_{29}H_{26}O_2$ requires C, 85·7; H, 6·4%); 1,1-*di*-p-*ethoxyphenyl*-3,3-*diphenylprop*-1-*ene*, m. p. 88—91° (Found: C, 85·5; H, 7·0. $C_{31}H_{30}O_2$ requires C, 85·7; H, 6·9%); 3,3-*diphenyl*-1,1-*di*-p-*propoxyphenylprop*-1-*ene* softens at 92° and melts at 96° (Found: C, 85·4; H, 7·0. $C_{33}H_{34}O_2$ requires C, 85·7; H, 7·4%); 3,3-*diphenyl*-1,1-*di*-p-*isopropoxyphenylprop*-1-*ene* softens at 97° and melts at 110° (Found: C, 85·5; H, 7·3%). Longer heating improved the yield only slightly, the 1,1-di-*p*-alkoxyphenylethylene being partly recovered and diphenylmethyl ethyl ether formed

1,1-*Di*-p-*methoxy*(*or ethoxy*)*phenyl*-3,3,3-*triphenylprop*-1-*ene*.—(*a*) Triphenylmethyl chloride (2·78 g., 0·01 mole) and 1,1-di-*p*-methoxyphenylethylene (2·4 g., 0·01 mole) or the ethoxyphenylethylene (2·68 g.) in dry benzene (30 c.c.) were refluxed for 3 hr. Hydrogen chloride was evolved and the colour changed from orange to green. Benzene was distilled off and a solution of the residue with potassium hydroxide (1 g.) in alcohol (30 c.c.) was refluxed for 30 min., then diluted with water (50 c.c.), cooled, and filtered. The solid was washed with water and recrystallised from alcohol, from which colourless 1,1-*di*-p-*methoxyphenyl*-3,3,3-*triphenylprop*-1-*ene* (1·6 g.), m. p. 137—138°, separated (Found: C, 87·0; H, 6·5. $C_{35}H_{30}O_2$ requires C, 87·1; H, 6·2%). 1,1-*Di*-p-*ethoxyphenyl*-3,3,3-*triphenylprop*-1-*ene* (yield 1·7 g.) had m. p. 136—137° (Found: C, 87·0; H, 6·4. $C_{37}H_{34}O_2$ requires C, 87·1; H, 6·7%).

(*b*) Experiment (*a*) was repeated but without the solvent. The mixture was heated in a boiling-water bath for 3 hr., melting and becoming yellow and then green with evolution of hydrogen chloride. The product was refluxed with alcoholic potassium hydroxide as in (*a*). 1,1-Di-*p*-methoxy(or ethoxy)phenyl-3,3,3-triphenylprop-1-ene was obtained. Increasing the time of reaction by 1 hr. only slightly improved the yield. The alcoholic mother-liquors gave unchanged dialkoxyethylene and a triphenylmethyl ethyl ether, m. p. and mixed m. p. 78° (cf. ref. 4).

1,1,3,3-*Tetra-aryl*-2-*bromopropenes*.—To the tetra-arylpropene (0·01 mole) in ether (30 c.c.), bromine (1·6 g., 0·01 mole) in ether (10 c.c.) was added. After evaporation the residue was recrystallised from alcohol–acetone (2 : 1). Thus were obtained as colourless crystals in almost quantitative yield: 2-bromo-1,1,3,3-tetraphenylpropene,[1a, b] m. p. 124° (Found: C, 76·1; H, 4·8; Br, 18·4. Calc. for $C_{27}H_{21}Br$: C, 76·2; H, 4·9; Br, 18·8%); 2-*bromo*-1,1-*di*-p-*methoxy*-, m. p. 96—97° (Found: C, 71·4; H, 5·0; Br, 16·8. $C_{29}H_{25}BrO_2$ requires C, 71·7; H, 5·2; Br, 16·5%), and 2-*bromo*-1,1-*di*-p-*ethoxy*-*phenyl*-3,3-*diphenylprop*-1-*ene*, m. p. 116—117° (Found: C,

[4] Hemilian, *Ber.*, 1874, **7**, 1203.

72·2; H, 5·7; Br, 16·1. $C_{31}H_{29}BrO_2$ requires C, 72·5; H, 5·7; Br, 15·6%); *2-bromo-3,3-diphenyl-1,1-di*-p-*propoxy-*, m. p. 80—82° (Found: C, 72·7; H, 6·1; Br, 15·2. $C_{33}H_{33}BrO_2$ requires C, 73·2; H, 6·1; Br, 14·8%), and *-isopropoxy-phenylprop-1-ene*, m. p. 129—130° (Found: C, 72·9; H, 6·1; Br, 15·2%).

Ozonolysis of Tetra-aryl-2-bromopropenes.—A stream of ozonised oxygen (*ca.* 3%) was passed through a cold solution of the tetra-aryl-2-bromopropene (0·5 g.) in carbon tetrachloride (30 c.c.) for 48 hr. Raney nickel sludge (*ca.* 5 g.) in distilled water was added and the mixture heated on the water-bath until carbon tetrachloride was recovered. The mixture was decanted and treated with 10% aqueous sodium hydroxide. The undissolved material was extracted with ether, the extract was washed with water and evaporated, and the residue recrystallised from alcohol to give benzophenone or the corresponding 4,4′-dialkoxybenzophenone (dimethoxy-, m. p. 142°; diethoxy-, m. p. 131°; dipropoxy-, m. p. 127°; di-isopropoxy-, m. p. 72°), showing no depression of the m. p. when mixed with authentic samples.[5] On acidification, the alkaline mother-liquor gave diphenylacetic acid, m. p. and mixed m. p. 144—145°.

Tetra-arylallenes.—This is exemplified by the preparation of tetraphenylallene. 2-Bromo-1,1,3,3-tetraphenylpropene (1 g.) and potassium hydroxide (2 g.) in alcohol (30 c.c.) were refluxed for 1 hr., then cooled and diluted with water (50 c.c.). The solid was washed with water and recrystallised from alcohol–acetone (2 : 1). It had m. p. 165° and was tetraphenylallene [1a] (yield almost quantitative) (Found: C, 93·8; H, 5·7. Calc. for $C_{27}H_{20}$: C, 94·2; H, 5·8%). Similarly were obtained in almost quantitative yield: 1,1-di-*p*-methoxyphenyl-3,3-diphenylallene, m. p. 104° (cf. Ziegler and Ochs [3]) (Found: C, 85·6; H, 6·0. Calc. for $C_{29}H_{24}O_2$: C, 86·1; H, 5·9%); *1,1-di*-p-*ethoxyphenyl-3,3-diphenyallene*, m. p. 109° (Found: C, 85·6; H, 6·4. $C_{31}H_{28}O_2$ requires C, 86·1; H, 6·5%); *3,3-diphenyl-1,1-di*-p-*propoxyphenylallene*, m. p. 73—74° (Found: C, 85·6; H, 7·1. $C_{33}H_{32}O_2$ requires C, 86·1; H, 7·0%); and *3,3-diphenyl-1,1-di*-p-*isopropoxyphenylallene*, m. p. 102—103° (Found: C, 85·7; H, 6·8%).

Department of Chemistry, Faculty of Science,
Cairo University, Egypt, U.A.R.

[*Received, December 15th*, 1960.]

[5] Jones, *J.*, 1936, 1854.

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528. *Quinazolines. Part I. Cations of Quinazoline.*

By Adrien Albert, W. L. F. Armarego, and E. Spinner.

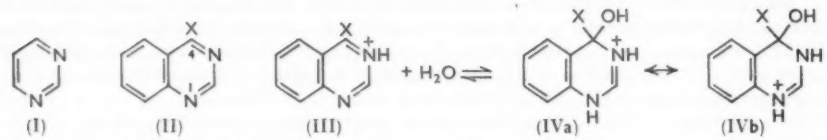
Depending on the conditions, quinazoline can form either a normal or an abnormal monocation; the latter preponderates in aqueous medium (4-substituted quinazolines form predominantly the normal monocation even in dilute aqueous acid). The abnormal ion is formed by the reaction of water with the normal ion; a possible structure is (IV; X = H) although some evidence at present appears not to be wholly in accord with this. A (normal) dication of quinazoline has also been obtained.

Whereas there is a great similarity in base strength [1] between pyridazine (pK_a 2·3) and cinnoline (2·3), and between pyrazine (0·6) and quinoxaline (0·7), there is a large difference between pyrimidine (I) (1·3) and quinazoline (II; X = H) (3·5); 4-methylquinazoline (2·5), by contrast, resembles 4-methylpyrimidine (2·0). Thus, quinazoline (predicted pK_a ~1·5) is an anomalously strong base. Ultraviolet spectra show that only the cation of quinazoline is abnormal: quinoline, isoquinoline, and the eight known diazanaphthalenes [2,3] all have ultraviolet spectra like that of naphthalene; and the spectra undergo but minor changes on cation formation,[4] with the exception of that of quinazoline (also that of 2-methylquinazoline [5]) which is greatly changed on cation formation in dilute aqueous acid (Fig. 1).

[1] (*a*) Albert, "Heterocyclic Chemistry," Athlone Press, London, 1959, pp. 344—345; (*b*) Albert, Goldacre, and Phillips, *J.*, 1948, 2240; (*c*) Albert, Brown, and Wood, *J.*, 1954, 3832.
[2] Ref. 1 (*a*), pp. 300, 314—316.
[3] Albert, *J.*, 1960, 1790.
[4] Ref. 1 (*a*), p. 303.
[5] Mason, communication to Osborn *et al.*; see ref. 7.

By contrast, the spectra of 4-methyl-[5] and 2,4-dimethyl-quinazoline are little changed under these conditions.

To explain the anomaly it has been suggested[6,7] that water adds covalently to the cation of quinazoline, the hydroxyl group becoming attached to the 4-position. Nucleophilic addition of water to C=N bonds has been observed previously, *e.g.*, to azomethines,[8] but only when such bonds are not part of an aromatic ring. (However, some quaternised pyridines,[9a] and even neutral acridine[9b] and quinoxaline,[10] add various nucleophilic reagents.) The addition of water to the normal cation of quinazoline (III; X = H) can



yield a product for which stabilization by amidinium resonance (IV,a ⟷ b) has been postulated.[6,7] Several 3-methylquinazolinium derivatives contain a very firmly held alcohol molecule[11,12] which, it has been suggested,[7] is covalently bound.

Two different hydrochlorides of quinazoline have now been prepared as solids. In anhydrous ether, quinazoline was converted into a hydrochloride $C_8H_7ClN_2$; this was very hygroscopic and readily formed a hydrate $C_8H_9ClN_2O$. The latter is stable at room temperature, and relatively difficult to dehydrate even in a vacuum at 60°; infrared spectra suggested that it contained covalently bound water, as it failed to show several bands observed for $C_8H_7ClN_2$ (see Table 1), and showed extra bands at 1474 and 1240 cm.$^{-1}$

TABLE 1. *The infrared spectra * of quinazoline hydrochloride and quinazoline hydrochloride " monohydrate."*

$C_8H_7N_2Cl$: 3250ms, 3090mw, 3025mw, 2980s, 1669ms, 1599w, 1582ms, 1495ms, 1448m, **1427**m, 1332ms, 1293m, 1264m, 1218ms, **1170**mw, 1159mw, 1123vw, 1039mw, 1024ms, 965mw, 955vw, **931**m, 872vw, **838**m, 805 + 799w, 774ms, 726vw, **663**m.

$C_8H_9N_2OCl$: 3350ms, 3100s, 2975mw, 2860m, 2750m, 1665ms, 1624ms, 1599w, 1570ms, 1495ms, **1474**m, 1441ms, 1329m, 1282vw, 1266vw, **1240**mw, 1211ms, 1156w, 1120w, 1027ms, **989**w, 966mw, 951 + 945w, 880vw, 811m, 798w, 767ms, 735vw.

* Wave-numbers of absorption peaks in cm.$^{-1}$; bands not common to both spectra are in bold type.

that are possibly attributable to CH and OH bending vibrations of the CH·OH group in (IV; X = H).

The Spectrum of Quinazoline in Acidic Media of Low Water Content.—In order to ascertain whether the anomaly in the ultraviolet spectrum of the cation of quinazoline is in fact associated with the presence of water, the spectrum of quinazoline was measured in anhydrous dichloroacetic acid which has[13] an acidic pK_a value of 1·0 in water and should not undergo nucleophilic addition to a system of double bonds. The Hammett acidity function, H_0, of pure dichloroacetic acid, determined with *o*-nitroaniline as the solute, is −0·9, hence a base with a pK_a value greater than +1 would be almost completely ionized in it.

In this solvent quinazoline gives a normal cation spectrum which closely resembles

[6] Albert, *Chem. Soc. Special Publ.* No. 3, 1955, p. 138; cf. ref. 1 (*a*), p. 121.
[7] Osborn, Schofield, and Short, *J.*, 1956, 4191.
[8] Dimroth and Zoeppritz, *Ber.*, 1902, **35**, 990; Gattermann, *Annalen*, 1907, **357**, 336; Carré and Baranger, *Bull. Soc. chim. France*, 1928, **43**, 73.
[9] (*a*) Burton and Kaplan, *J. Biol. Chem.*, 1954, **206**, 283; **211**, 447; Eys and Kaplan, *J. Biol. Chem.*, 1957, **228**, 305; (*b*) Kröhnke and Honig, *Annalen*, 1959, **624**, 97.
[10] Bergstrom and Ogg, *J. Amer. Chem. Soc.*, 1931, **53**, 245.
[11] Gabriel and Colman, *Ber.*, 1904, **37**, 3643.
[12] Schöpf and Oechler, *Annalen*, 1936, **523**, 1.
[13] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.

that of 4-methylquinazoline and shows the characteristic band near 330 mμ which is absent from the quinazoline cation spectrum in dilute aqueous acid (see Table 3).

In concentrated sulphuric acid both quinazoline and its 4-methyl derivative form (stable) dications which possess normal spectra (see Table 3). The most illuminating spectra, however, are those obtained in rather concentrated aqueous sulphuric acid. The behaviour of 4-methylquinazoline is straightforward. At low acid strength (H_0 values to $-2{\cdot}5$) only the spectrum of the monocation is seen, at high acid strengths (H_0 $-6{\cdot}5$ to $-9{\cdot}4$) only the dication, and at intermediate acid strengths these two species are present in equilibrium with each other, their relative proportions varying with H_0 corresponding to proton addition to a base with a pK_a value of $-4{\cdot}4 \pm 0{\cdot}2$.

In solutions of quinazoline in sulphuric acid–water mixtures, however, *three* ionic species are observable, *viz.*: at H_0 -1 the abnormal monocation predominates; at

FIG. 1. *Ultraviolet spectra, in water, of* (A) *quinazoline* (pH 7); (B) *the abnormal cation of quinazoline* (pH 1); (C) *the cation of 4-methylquinazoline* (pH 0).

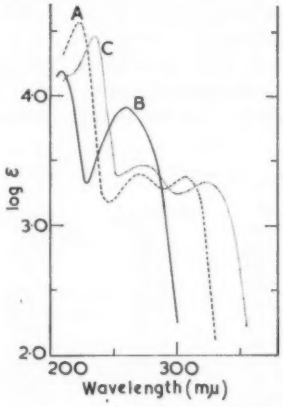
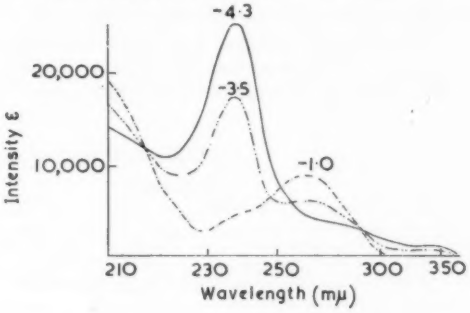


FIG. 2. *Ultraviolet spectra of solutions of quinazoline in sulphuric acid–water mixtures, at Hammett acidity functions* (H_0) *of* $-1{\cdot}0$, $-3{,}5$, *and* $-4{\cdot}5$.



H_0 $-7{\cdot}0$ to $-9{\cdot}4$ the (normal) dication is seen; but at H_0 $-4{\cdot}3$ the spectrum resembles that of 4-methylquinazoline in dilute aqueous acid, and the main species present must be the *normal* (anhydrous) monocation of quinazoline (III; X = H) already observed in anhydrous dichloroacetic acid. The value deduced for the second basic ionization constant, pK_a $-5{\cdot}5 \pm 0{\cdot}2$, as compared with $-6{\cdot}3 \pm 0{\cdot}2$ obtained for pyrimidine and $-4{\cdot}4 \pm 0{\cdot}2$ for 4-methylquinazoline, also agrees with the view that the equilibrium is mainly one between the normal dication and the normal monocation of quinazoline.

The percentage of normal monocation present increases with increasing acid strength, only slightly at low values of $-H_0$, but very markedly at higher values. The equilibrium is illustrated in Fig. 2. The estimated percentage of normal monocation present is 1—2% at H_0 $-1{\cdot}0$, 50—60% at H_0 $-3{\cdot}5$, and 80—90% at H_0 $-4{\cdot}3$ (where about 7% of the dication is also present). In mixtures of sulphuric acid and water containing more than 38% of acid ($-H_0 > 2{\cdot}3$) the activity of water is much lower than its stoicheiometric concentration would suggest, because the inner solvation shells (of water molecules held very firmly around the H_3O^+ and HSO_4^- ions) are depleted. It is therefore reasonable that in concentrated aqueous sulphuric acid an equilibrium such as that between (III; X = H) and (IV; X = H) should be strongly dependent on the solvent composition.

4-Substituted Quinazolines.—There is thus abundant evidence that the normal (anhydrous) cation of quinazoline is capable of existence, but in dilute aqueous acid it is

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not the energetically preferred species. In the case of 4-methylquinazoline, on the other hand, only the normal cation (III; X = Me) is known. It must now be decided whether this resistance to hydration is due to the (weak) electron-donating effect or to the steric effect of the methyl group. Electronic effects are known to be of importance, because the (strongly electron-donating) amino-group, if present in any position in quinazoline other than at 6, causes the normal cation to predominate.[7]

However, 4-chloro-, 4-cyano-, and 4-cyanoethoxycarbonylmethyl-quinazoline, in 5·6N-hydrochloric acid, have now also been found to give mainly the normal cations (see Table 3), although here the substituent is electron-withdrawing. It is thus by their steric effect that 4-substituents cause predominance of the normal cation, and the view that the conversion of the normal into the abnormal cation involves attack at the 4-position is confirmed.

4-Cyanoethoxycarbonylmethylquinazoline is stable in 5·6N-hydrochloric acid, but the cyano- and the chloro-derivative are rapidly hydrolysed to 4-hydroxyquinazoline (the half-reaction times being about 5 min. and 50 sec., respectively). Very probably a small amount of an ion (IV) is present in equilibrium with (III) here; however, amide cyanohydrins and chlorohydrins are not stable, and rapid elimination of hydrogen cyanide or hydrogen chloride from a form (IV; X = CN or Cl), with formation of the cation of 4-quinazolone (*i.e.*, of 4-hydroxyquinozaline), would be expected.*

Unsuccessful attempts were made to synthesize 4-acetonyl- (II; X = CH_2·COMe) and 4-cyanomethyl-quinazoline (II; X = CH_2·CN) as examples of quinazolines in which the "X" group is electron-attracting but not readily hydrolysable. In the former synthesis

TABLE 2. *Ionization constants in water, at* 20°.

Compound	pK_a	Spread (±)	Concn. (M)
Quinazoline [a] (II; X = H)	3·51	0·05	0·07
2-Methylquinazoline	4·52	0·02	0·005
4-Methylquinazoline [a]	2·52	0·02	0·07
2,4-Dimethylquinazoline	3·60	0·01	0·002
4-(α-Cyano-α-ethoxycarbonylmethyl)quinazoline	(9·78	0·05	0·005) [b]
3,4-Dihydroquinazoline	9·19	0·07	0·002
3,4-Dihydro-3-methylquinazoline	9·23	0·03	0·001
1,4-Dihydro-1-methylquinazoline	9·43	0·04	0·005
3,4-Dihydroquinazolinium-4-sulphonate (VI)	(7·1		0·002) [b,c]
3,4-Dihydro-2-methylquinazoline	10·16	0·04	0·005
1,2 3,4-Tetrahydroquinazoline	7·65	0·03	0·005
Phthalazine	3·50	0·02	0·005
1-Methylphthalazine	4·39	0·01	0·005

[a] Albert, Brown, and Wood, *J.*, 1954, 3832. [b] Proton lost; the other pK_a value is less than 1. [c] Approx.; the anion splits off sulphite ion at an appreciable rate.

benzyl sodioacetoacetate was condensed with 4-chloroquinazoline with the aim of later debenzylation and decarboxylation; however, the condensation followed the mechanism suggested by Elderfield and Serlin [14] and 4-benzyloxycarbonylmethylquinazoline and not 4-α-benzyloxycarbonylacetonylquinazoline was isolated. In the latter synthesis alkaline hydrolysis of 4-(α-cyano-α-ethoxycarbonylmethyl)quinazoline was studied but the ester resisted hydrolysis when boiled with 3 equivalents of alkali and with 3N-potassium hydroxide; this is probably due to the formation of a stable salt (cf. pK_a in Table 2), and more drastic hydrolytic conditions caused considerable decomposition. Finally 4-(α-cyano-α-benzyloxycarbonylmethyl)quinazoline was prepared, but on hydrogenolysis a mixture was obtained from which the free acid could not be isolated.

Ionization Constants.—2-Methylquinazoline has an anomalously high base strength,

* Some other 4-substituted quinazolines [*e.g.*, where X = $CEt(CO_2Et)_2$] give 4-hydroxyquinazoline when heated with acid,[14] presumably by the same mechanism.

[14] Elderfield and Serlin, *J. Org. Chem.*, 1951, **16**, 1669.

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TABLE 3. *Ultraviolet spectra.*

Compound	Solvent	pH (or H_0)	Species [a]	$\lambda_{max.}$ (mμ) (inflections in italics)	log $\varepsilon_{max.}$
Quinazoline	H_2O	7·0	N	222; 271; 305	4·57; 3·40; 3·38
	H_2O	1·0	AC	208; 260	4·20; 3·91
	$CHCl_2{\cdot}CO_2H$ [b]	−0·9	C	297; *309*; 333	3·44; *3·36*; 3·36
	H_2O–H_2SO_4	−4·3	C	238; *284*; *299*; *309*; 333	4·40; *3·51*; *3·30*; *3·22*; 3·10
	H_2SO_4	−9·4	DC	252; 307; *314*; 363	4·54; 3·57; *3·55*; 3·10
4-Methylquinazoline	H_2O	7·0	N	223; 270; 305; 314	4·62; 3·45; 3·45; 3·41
	H_2O	0·3	C	234; 270; 279; 323	4·52; 3·47; 3·45; 3·34
	$CHCl_2{\cdot}CO_2H$ [b]	−0·9	C	298; 328	3·41; 3·44
	H_2SO_4	−9·4	DC	253; 305; *313*; 353	4·50; 3·55; *3·54*; 3·20
Pyrimidine	H_2O–H_2SO_4	−3·6	C [c, d]	*238* + 242 + *248*	*3·57* + 3·64 + *3·52*
	H_2O–H_2SO_4	−8·9	DC [d, e]	*242* + 246 + *252*	*3·73* + 3·77 + *3·62*
2-Methylquinazoline	H_2O	7·0	N	223; 268; 310; *320*	4·60; 3·41; 3·40; *3·31*
	H_2O	1·0	AC	207; 258	4·28; 3·96
2,4-Dimethylquinazoline	H_2O	7·0	N	226; 266; 309; *318*	4·67; 3·45; 3·49; *3·45*
	H_2O	1·0	C	236; 265; *277*; *302*; 322	4·46; 3·49; *3·45*; *3·29*; 3·29
4-Chloroquinazoline [f]	H_2O	5·5	N	228; 274; 309; *317*	4·62; 3·41; 3·50; *3·47*
	H_2O–HCl	−1·9	C [g]	242; 310	4·62; 3·75
4-Cyanoquinazoline [f]	H_2O	7·0	N	237; 324	4·49; 3·58
	H_2O–HCl	−1·9	C	246; 328	4·39; 3·78
4-(α-Cyano-α-ethoxycarbonylmethyl)-quinazoline	H_2O–EtOH (1 : 1)	7·0	N	209; 234 + 239 285 + *292*; 348; 363 + 382	4·54; 3·88 + 3·89 3·97 + *3·95*; 4·17; 4·39 + 4·36
	H_2O–HCl	−1·9	C	216; 238 + 244; 282; *343*; 358 + 376	4·33; 3·84 + 3·86; 4·26; *4·23*; 4·40 + 4·36
3,4-Dihydroquinazoline	H_2O	11·5	N	*217* + 221 + *227*; 291	*4·07* + 4·09 + *3·97*; 3·76
	H_2O	7·0	C	212 + 217 + *225*; 280	4·26 + 4·25 + *4·01*; 3·69
3,4-Dihydro-3-methylquinazoline	H_2O	11·5	N	219 + 225 + 231; 304	*3·99* + 4·01 + 4·04; 3·90
	H_2O	7·0	C	214 + 218 + *224*; 284	4·23 + 4·24 + *4·04*; 3·79
1,4-Dihydro-1-methylquinazoline	H_2O	11·5	N	? [h] + *220* + *225*; 289	? + *4·04* + *3·97*; 3·64
	H_2O	7·0	C	213 + 218 + *224*; 282 + 292	4·20 + 4·19 + *3·99*; 3·61 + 3·60
3,4-Dihydro-2-methylquinazoline	H_2O	12·5	N	*217* + 220 + *226*; 290	*4·12* + 4·13 + *4·02*; 3·82
	H_2O	7·0	C	211 + 215 + *221*; 276	4·30 + 4·31 + *4·08*; 3·74
3,4-Dihydroquinazolinium-4-sulphonate (VI)	H_2O	4·0	"N" [i]	222 + *229*; 282	4·17 + *3·93*; 3·66
1,2,3,4-Tetrahydroquinazoline	H_2O	10	N	239; 287	3·80; 3·19
		5	C	237; 287	3·82; 3·16
Phthalazine	H_2O	7	N	218; 261; 292; *297*; 305	4·83; 3·53; 3·18; *3·11*; 3·11
	H_2O	0	C	229; 273; 314	4·61; 3·35; 3·45
1-Methylphthalazine	H_2O	7	N	219; 262; *270*; 292; 305	4·70; 3·59; *3·57*; 3·21; 3·18
	H_2O	2	C	230; 271; *304*; 312	4·62; 3·40; *3·40*; 3·46

[a] N = neutral molecule; C = (normal) cation; AC = abnormal cation; DC = dication. [b] Transmission limit, 290 mμ. [c] This spectrum is practically unchanged between H_0 −1·12 and H_0 −4·5. [d] Near H_0 −6·3 pyrimidine shows only a broad uninflected band ($\lambda_{max.}$ ~243·5 mμ). [e] The wavelength of this spectrum is only slightly changed between $H_0 = -8{\cdot}5$ ($\lambda_{max.}$ 246 mμ) and −9·35 ($\lambda_{max.}$ 245·5 mμ). [f] Estimated basic pK_a value between 0 and −0·5. [g] Determined within about 2 seconds after acidification (by mixing in a specially designed apparatus utilising a rapid-flow technique; see acknowledgments). [h] Peak below 210 mμ. [i] Zwitterion (VI).

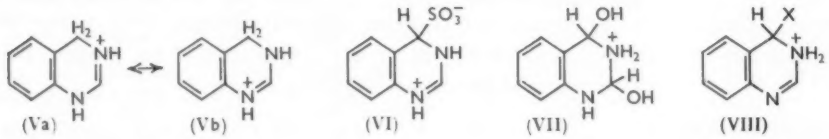
but the 2,4-dimethyl derivative has not, in agreement with the view that abnormal cation formation entails attack on an unhindered 4-position.

Spectral Shifts.—When substance (II; X = H, Me, Cl, or CN) forms the normal monocation, there is a small shift of the whole electronic spectrum to longer wavelengths; formation of the dication (when X = H or Me) results in a bigger shift, in the same direction.

As regards substituent effects (relative to that of hydrogen), the spectrum of neutral quinazoline is displaced to longer wavelengths by 4-substituents in the order (H <)Me < Cl < CN. However, 4-substituents in the normal monocation (III) displace the long-wavelength band (near 330 mμ) to *shorter* wavelengths, which is very remarkable; the displacements increase in the order (H <)CN < Me < Cl. The long-wavelength band in the dication is similarly moved to shorter wavelengths when $H_{(4)}$ is replaced by Me.

The group $-CH(CN)\cdot CO_2Et$ in the 4-position of quinazoline greatly modifies, and complicates, the spectrum. There is complete correspondence between the bands observed for the cation and those appearing for the neutral molecule, but cation formation does not affect the whole spectrum uniformly.

Spectral Comparison between the Abnormal Monocation of Quinazoline and Substances related to Reduced Quinazolines.—That the formation of the abnormal cation of quinazoline does not entail ring fission is indicated by: (*a*) the very rapid reversibility of abnormal cation formation; (*b*) the electronic spectrum of the abnormal cation, which is not what would be expected for an *ortho*-substituted aniline or an *ortho*-substituted benzaldehyde (either of which should show an absorption maximum above 290 mμ); (*c*) the ready oxidation of quinazoline in 2N-sulphuric acid (in which ~98% is present as the abnormal cation), by hydrogen peroxide or chromic acid at 20°, giving a high yield of 4-hydroxyquinazoline (cf. a similar demonstration of covalent hydration in 2- and 6-hydroxypteridine [15]).



If, on the other hand, the structure of the abnormal cation is given by (IV), its spectrum should be similar to that of the cation (V) of 3,4-dihydroquinazoline; the replacement of a hydrogen atom in the saturated portion of (V) by hydroxyl should only produce small band shifts. Actually, there is a general resemblance between the two spectra (see Table 3); however, the band of the cation (V) at 280 mμ appears to be displaced to 260 mμ in the abnormal quinazolinium ion, *i.e.*, the shift is too large to be wholly in accord with structure (IV) for the ion.

In order to ascertain the effect of substituents on the spectrum of the cation (V), we examined the 1-, 2-, and 3-methyl derivatives of the cation (V), also the product (VI) of nucleophilic addition of sulphurous acid to quinazoline. The spectra of all these resemble that of the cation (V) closely, the above-mentioned band maximum being located near 282 mμ. Thus a 4-hydroxyl group in the cation (V) is unlikely to produce a hypsochromic shift of 20 mμ, and this throws further doubt on the proposed structure (IV) for the abnormal cation.

It is also conceivable that the abnormal cation is the dihydrate (VII), formed by addition of two molecules of water to the normal ion (III; X = H). However, the cation of 1,2,3,4-tetrahydroquinazoline has a spectrum closely resembling that of aniline (as expected), and quite different from that of the abnormal quinazoline ion, for which structure (VII) is therefore ruled out.

Regarding other possibilities, the abnormal ion could have structure (VIII; X = OH), but this seems very unlikely because, for the cations of 3,4-dihydroquinazoline and its 3-methyl and 4-sulphonate derivatives, the tautomers of type (V) and (VI) are energetically preferred to (VIII). Alternatively, the relative contributions of the canonical forms (a) and (b) could be different for the ion (IV) on the one hand, and the ion (V) and the *N*-methyl and 4-sulphonate derivatives on the other; but this, too, is somewhat unlikely.

[15] Brown and Mason, *J.*, 1956, 3443.

However, there is no conclusive evidence in this regard, and the precise structure of the abnormal quinazoline cation is still unsettled; it is hoped that further work will shed more light on it.

The Structure of " **3,4** *"-Dihydroquinazoline.*—This is not settled unambigously from the syntheses because prototropic rearrangement, giving the 1,4-dihydro-tautomer, could have occurred. Also the similarity in base strength between 1,4-dihydro-1-methyl- and 3,4-dihydro-3-methyl-quinazoline suggests that in aqueous solution "3,4"-dihydroquinazoline could be appreciably tautomerized to the 1,4-dihydro-isomer. However, the electronic spectrum of the substance, especially in the short-wavelength region (peak at 221 mμ), resembles that of 3,4-dihydro-3-methylquinazoline (double peak at 225 + 231 mμ) more closely than that of 1,4-dihydro-1-methylquinazoline (peak not observed because below 210 mμ).* It is therefore concluded that this substance is probably largely 3,4- rather than 1,4-dihydroquinazoline.

The Cation of Phthalazine.—The only other instance of a diazanaphthalene with a considerably higher base strength than that of its parent diazine is phthalazine (2,3-diazanaphthalene), its pK_a value being 3·5 as compared with 2·3 for pyridazine. This could simply be due to the high single-bond character of the N–N bond in phthalazine and it is to be noted that, while a stronger base than cinnoline (pK_a 2·3), phthalazine is still a much weaker base than isoquinoline (pK_a 5·4). The alternative possibility that phthalazine might form an abnormal cation, like quinazoline, is ruled out by the electronic spectrum of the phthalazine cation which is now shown to be normal and similar to that of 1-methylphthalazine (see Table 3).

Experimental

Analyses were by Dr. J. E. Fildes and her staff.

Syntheses of Compounds.—Quinazoline [16] and its 2-methyl-,[17] 4-methyl-,[18] 2,4-dimethyl-,[19] 4-(α-cyano-α-ethoxycarbonylmethyl)-,[14] 4-chloro-,[20] 3,4-dihydro-,[17] 3,4-dihydro-3-methyl-,[11] 1,4-dihydro-1-methyl-,[21] 3,4-dihydro-2-methyl-,[21] and 1,2,3,4-tetrahydro-derivative,[22] phthalazine,[23] and 1-methylphthalazine [24] were prepared as described in the literature, examined chromatographically, and purified for analysis.

Quinazoline hydrochloride. Dry hydrogen chloride was bubbled through a solution of quinazoline (500 mg.) in anhydrous ether (30 ml.) until separation of the white needles was complete. The apparatus was flushed with dry nitrogen and filtration carried out in a dry box. The anhydrous salt was heated at 100° for 15 min. to remove excess of hydrogen chloride. This product readily absorbed atmospheric moisture, almost liquefying, then resolidifying, to give a non-hygroscopic salt (71%), m. p. 127—128°, which contained the elements of water (Found: C, 52·2; H, 4·9; Cl, 19·3. $C_8H_9ClN_2O$ requires C, 52·05; H, 4·9; Cl, 19·2%). It was not dehydrated at 25°/15 mm. (over KOH) in 4 days, but lost 58% of its water at 60°/15 mm. (over P_2O_5) in 16 hr.

3,4-Dihydroquinazolinium-4-sulphonate. A 10% solution of sodium sulphite in water was added to aqueous quinazoline (650 mg. in 1 ml. of water) and the whole was left at 20—25° for 1 hr. The white solid (A) was filtered off, triturated with water, then with a little ethanol, and dried (882 mg., 76%). It had m. p. 181—182° (effervescence) and contained sodium. Recrystallisation from boiling water gave white needles (B) which sublimed at 210—212° [lit.,[25]

* Whatever the structure of the substance, a bathochromic shift is expected for the corresponding *N*-methyl derivative.

[16] Bogert and McColm, *J. Amer. Chem. Soc.*, 1927, **49**, 2650.
[17] Bischler and Lang, *Ber.*, 1895, **28**, 279.
[18] Schofield and Swain, *J.*, 1949, 1367.
[19] Bogert and Nabenhauer, *J. Amer. Chem. Soc.*, 1924, **46**, 1932.
[20] Endicott, Wick, Mercury, and Sherrill, *J. Amer. Chem. Soc.*, 1946, **68**, 1299.
[21] Part II, following paper.
[22] Gabriel, *Ber.*, 1903, **36**, 811.
[23] Stephenson, *Chem. and Ind.*, 1957, 174.
[24] Dr. E. F. M. Stephenson, personal communication.
[25] Tomisek and Christiansen, *J. Amer. Chem. Soc.*, 1945, **67**, 2112.

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195—199° (decomp.)] (Found: C, 45·2; H, 4·1; N, 13·1; S, 15·3; Ash, 0. Calc. for $C_8H_8N_2O_3S$: C, 45·3; H, 3·8; N, 13·2; S, 15·1%). Materials (A) and (B) have identical R_F values at pH 5.

4-Cyanoquinazoline. This was obtained in 2% yield by fusing 4-chloroquinazoline with cuprous cyanide, although it had been claimed [25] that no cyanoquinazoline could be obtained by this method. It was also prepared in the same overall yield, by converting 4-chloroquinazoline into trimethyl-4-quinazolinylammonium chloride and fusing the latter with sodium cyanide in acetamide according to the general method of Klötzer.[26] 4-Cyanoquinazoline had m. p. 115—116° (lit.,[25] 118—119°) (Found: C, 69·9; H, 3·5; N, 26·8. Calc. for $C_9H_5N_3$: C, 69·7; H, 3·25; N, 27·1%). These specimens proved to be identical with the cyanoquinazoline prepared recently, in better yield, by Higashino [27] by oxidation of the quinazoline–hydrogen cyanide adduct.

4-Benzyloxycarbonylmethylquinazoline. 4-Chloroquinazoline (3·5 g., 1 mol.) in dry benzene (75 ml.) was added slowly to a stirred suspension of benzyl sodioacetoacetate [prepared from 480 mg. of sodium and 3·84 g. of benzyl acetoacetate [28] in ether; the solvent was then removed *in vacuo*] in dry benzene (75 ml.). The mixture was stirred and refluxed for 28 hr. The solvent was distilled off and the residue dissolved in the minimum volume of water and acidified to pH 2. The precipitated *ester* (3·1 g., 52%) recrystallised from benzene–light petroleum (b. p. 40—60°) as needles, m. p. 139—140° (Found: C, 73·6; H, 5·1; N, 9·9. $C_{17}H_{14}N_2O_2$ requires C, 73·4; H, 5·1; N, 10·1%).

4-(α-Cyano-α-benzyloxycarbonylmethyl)quinazoline. To a stirred solution of 4-chloroquinazoline (6·6 g., 1 mol.) in dry benzene (70 ml.) was added a suspension of benzyl sodiocyanoacetate (from 925 mg. of sodium and 7·0 g. of benzyl cyanoacetate [29]) in dry benzene (125 ml.). The mixture was refluxed for 25 hr. and worked up as above. The *ester* (5·4 g., 44%) crystallised from benzene–light petroleum (b. p. 40—60°) as needles, m. p. 150—151° (Found: C, 71·35; H, 4·4; N, 13·8. $C_{18}H_{13}N_3O_2$ requires C, 71·3; H, 4·3; N, 13·9%).

Oxidation of the Abnormal Quinazoline Cation.—Hydrogen peroxide (100-vol.; 2·3 ml., 2 equiv.) was added to a solution of quinazoline (1·30 g., 1 mol.) in 2N-sulphuric acid (10 ml.). After 2 days at room temperature the solution was made alkaline (pH ~10) and then acidified to pH ~4 with glacial acetic acid. 4-Hydroxyquinazoline gradually separated; recrystallised from ethanol–light petroleum (b. p. 40—60°), it (1·21 g., 83%) had m. p. alone or mixed with 4-hydroxyquinazoline 217—218°. Paper chromatography in 3% aqueous ammonium chloride and in butan-1-ol–5N-acetic acid (3 : 1) showed that the two substances were identical and that no quinazoline was left in the mother-liquors. Oxidation of quinazoline in 2N-sulphuric acid with chromic oxide (4 equiv.) gave 4-hydroxyquinazoline which was isolated in 95% yield.

Ionization Constants.—In the range pK_a 1—12·5 these were measured by the potentiometric method.[30] Second basic ionization constants were determined spectrophotometrically.

Spectra.—Infrared spectra were taken with a Perkin–Elmer 21 double-beam spectrophotometer, ultraviolet spectra with a Perkin–Elmer Spectracord model 4000-A double-beam spectrophotometer, and the maxima checked with a Hilger Uvispek Mark V manual instrument.

We thank Dr. D. J. Brown for a specimen of pyrimidine, Dr. D. D. Perrin for examining 4-chloroquinazoline by his rapid-flow technique, and Messrs. D. T. Light, F. V. Robinson, and K. Tratt for technical assistance.

Department of Medical Chemistry, Institute of Advanced Studies,
Australian National University,
Canberra, A.C.T., Australia. [*Received, November 7th*, 1960.]

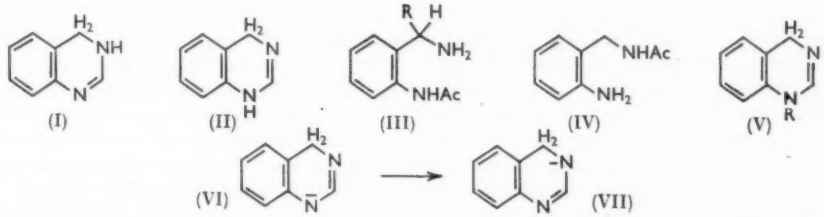
[26] Klötzer, *Monatsh.*, 1956, **87**, 131.
[27] Higashino, *J. Pharm. Soc. Japan*, 1960, **80**, 245.
[28] Bacon and Shaklee, *Amer. Chem. J.*, 1905, **33**, 79.
[29] Newman, Magerlein, and Wheatley, *J. Amer. Chem. Soc.*, 1946, **68**, 2112.
[30] Albert and Phillips, *J.*, 1956, 1294.

529. *Quinazolines. Part II.*[1] 1,4- *and* 3,4-*Dihydroquinazoline.*

By W. L. F. Armarego.

Syntheses of 1,4-dihydro-1-methyl and 1-benzyl-1,4-dihydro-quinazoline are described. Surprisingly, debenzylation of the latter gave 3,4-dihydroquinazoline. The dihydro-compound obtained by catalytic reduction of 2-methylquinazoline has been shown to be 3,4-dihydro-2-methylquinazoline. It is identical with the supposedly isomeric bases prepared by Bischler and by Gabriel and Jansen.

Dihydroquinazoline, obtained by the catalytic reduction of quinazoline,[2] can be regarded as a cyclic formamidine which may be 3,4- (I) or 1,4-dihydroquinazoline (II). As with the dihydronaphthalenes,[3] the 3,4-dihydroquinazoline seems to be more stable to prototropic change than the 1,4-isomer because the dihydroquinazoline obtained by reducing quinazoline has now been shown by direct methylation to be mainly, or maybe entirely, the 3,4-isomer. In order to make a more direct comparison, the synthesis of 1,4-dihydroquinazoline was attempted.



Although 3,4-dihydroquinazolines have long been known [4] and Carrington reported the synthesis of some 1,2-dihydroquinazolines in 1955,[5] only two 1,4-dihydroquinazolines are claimed in the literature. These are 1,4-dihydro-2-methyl- and 2,4-dimethyl-quinazoline which Bischler [6] prepared by cyclisation of the acetyl derivatives (III; R = H or Me). The constitution of this " 1,4-dihydro-2-methylquinazoline " was assigned (incorrectly as will be shown *) on the grounds that it appeared to differ from the dihydro-2-methylquinazoline prepared by Gabriel and Jansen [7] by dehydration of the amide (IV). Gabriel and Jansen [8] proved that their substance was the 3,4-dihydro-derivative since on methylation it gave 3,4-dihydro-2,3-dimethylquinazoline identical with that prepared unambiguously. Ried and Stahlhofen [9] also obtained what they claimed to be 3,4-dihydro-2-methylquinazoline by catalytic reduction of " 2-methyl-6,7-benzo-3,1,4-oxadiazepine " (now known to be 2-methylquinazoline 3-oxide [10]) and, although this dihydro-compound agreed in many respects with that of Gabriel and Jansen, its picrate melted 17° higher.

These compounds were synthesised by us for comparison. For the Bischler synthesis *o*-acetamidobenzaldoxime was prepared more conveniently from *o*-nitrobenzaldehyde

* However, Beilstein's " Handbuch der Organischen Chemie " (1944, **23**, pp. 155, 169) misquotes Bischler's compounds as 3,4-dihydro-derivatives.

[1] Part I, preceding paper.
[2] Bogert and Marr, *J. Amer. Chem. Soc.*, 1935, **57**, 729; Higashino, *J. Pharm. Soc. Japan*, 1960, **80**, 245.
[3] Roth and von Auwers, *Annalen*, 1915, **407**, 145; Williams, *J. Amer. Chem. Soc.*, 1942, **64**, 1395.
[4] Paal and Busch, *Ber.*, 1889, **22**, 2683.
[5] Carrington, *J.*, 1955, 2527.
[6] Bischler, *Ber.*, 1893, **26**, 1891.
[7] Gabriel and Jansen, *Ber.*, 1890, **23**, 2807.
[8] Gabriel and Jansen, *Ber.*, 1891, **24**, 3091; Gabriel, *Ber.*, 1903, **36**, 800.
[9] Ried and Stahlhofen, *Chem. Ber.*, 1954, **87**, 1814.
[10] Sternbach, Kaiser, and Reeder, *J. Amer. Chem. Soc.*, 1960, **82**, 457.

diacetate which was converted into *o*-nitrobenzaldoxime and then reduced catalytically to the amine which was acetylated. The *o*-acetamidobenzaldoxime was reduced and cyclised as before.[6] In the Gabriel–Jansen synthesis [*o*-nitrobenzylamine ⟶ *o*-(acetamidomethyl)nitrobenzene ⟶ *o*-acetamidomethylaniline ⟶ 3,4-dihydro-2-methylquinazoline] the nitro-compound was reduced catalytically instead of with zinc and acid. The two dihydro-bases had the same b. p. and ultraviolet spectra and gave the same hydrochloride (with very similar pK_a values) and the same picrate. Both picrates were dimorphic and the lower-melting (189—190°) was formed directly from the hydrochloride or free base and was converted after several recrystallisations into the more stable, higher-melting form (203—204°). This removes the only anomaly between the work of Gabriel and Jansen and that of Ried and Stahlhofen.

By comparison with quinazoline, 2-methylquinazoline should also be reduced to 3,4-dihydro-2-methylquinazoline. In the catalytic reductions we found that whereas quinazoline is hydrogenated to its dihydro-derivative with Adams platinum at atmospheric pressure, 2-methylquinazoline resisted reduction. This is probably due to poisoning of the platinum since 5% palladium–charcoal smoothly reduced 2-methylquinazoline to a dihydro-derivative, identical with that obtained by syntheses as above. The R_F values of the three bases when run together in two different solvent systems were the same. These bases are thus all 3,4-dihydro-2-methylquinazoline. Further, the ultraviolet spectrum of the last sample resembles more closely that of 3,4-dihydroquinazoline (and 3,4-dihydro-3-methylquinazoline) than that of 1,4-dihydro-1-methylquinazoline (cf. ref. 1).

The second " 1,4-dihydro "-compound prepared by Bischler was undoubtedly 3,4-dihydro-2,4-dimethylquinazoline and thus no 1,4-dihydroquinazoline was known before the 1,4-dihydro-1-methylquinazoline[1] which will now be described. *N*-Methylanthranilic acid was converted, *via* the isatoic anhydride, into *o*-methylaminobenzamide[11] which was reduced with lithium aluminium hydride to *o*-methylaminobenzylamine and this, after formylation, was cyclised to the base (V; R = Me).

On the other hand, the base (V; R = CH_2Ph) resisted catalytic hydrogenolysis with 10% palladium charcoal (although debenzylation of tertiary benzylamine is easy[12]), and 25% hydrobromic acid in glacial acetic acid opened the heterocyclic ring to give 2-(*N*-benzylformamido)benzylamine; but debenzylation with sodium in liquid ammonia unexpectedly gave 3,4-dihydroquinazoline (in 70% yield). This reaction could be due to conversion of the anion (VI) into the anion (VII) followed by addition of a proton on $N_{(3)}$, or, addition of a proton on $N_{(1)}$ followed by a prototropic change. The latter mechanism is less likely in the circumstances, but whichever takes place the postulated higher stability of the 3,4-dihydro-isomer is confirmed.

Experimental

Paper Chromatography.—The ascending technique was used with Whatman paper No. 1 and solvent system (A) (3% aqueous amonium chloride) or (B) (5N-acetic acid–butan-1-ol, 1 : 3). The radiation at 254 mμ from a mercury lamp with a " Chance Brothers " OX7/19874 filter was used to detect the fluorescent spots. Non-fluorescent spots were revealed by placing over the irradiated chromatogram a Perspex screen coated with a fine spray of cadmium borate suspended in chloroform. A pink background was obtained and the spots were deep blue. Ionisation constants were determined potentiometrically in water at 20°.[13]

3,4-Dihydro-2-methylquinazoline.—(a) *By catalytic reduction.* 2-Methylquinazoline (2·0 g.) in ethanol (50 ml.) and 5% palladium–charcoal (1·0 g.) was shaken with hydrogen at 713 mm. (absorption of 1 mol.). After filtration and evaporation the residue was distilled (b. p. 126—127°/0·9 mm.; 1·2 g., 60%); the distillate crystallised slowly. It had $\lambda_{max.}$ 220·5, 290 mμ (log ε 4·13, 3·82 in aqueous buffer of pH 12·3) and 211, 215, 276 mμ (log ε 4·30, 4·31, and 3·74

[11] Heilbron, Kitchen, Parkes, and Sutton, *J.*, 1925, **127**, 2171
[12] Hartung and Simonoff in " Organic Reactions," Wiley, New York, 1953, Vol. III, p. 277.
[13] Albert and Phillips, *J.*, 1956, 1294.

in aqueous buffer of pH 7·0) (Found: C, 73·4; H, 7·1. Calc. for $C_9H_{10}N_2$: C, 73·9; H, 6·9%), and R_F in (A) 0·75 and in (B) 0·53. It gave a hydrochloride, needles (from ethanol), m. p. 286—290° (decomp.), pK_a 10·17 ± 0·04 (M/200) (Found: C, 59·2; H, 5·9; N, 15·2; Cl, 19·4. Calc. for $C_9H_{10}N_2$,HCl: C, 59·2; H, 6·0; N, 15·3; Cl, 19·5%), and a picrate, m. p. 189—190°, needles from ethanol or water (Found: C, 48·1; H, 3·4; N, 18·8. Calc. for $C_{15}H_{13}N_5O_7$: C, 48·0; H, 3·5; N, 18·7%). The higher-melting picrate had m. p. 203—204° (rosettes from ethanol; lit.,[9] 204—205°) (Found: C, 47·8; H, 3·4; N, 18·6%).

o-*Nitrobenzaldoxime.*—*o*-Nitrobenzaldehyde diacetate [14] (40 g.) in ethanol (200 ml.) was refluxed in aqueous hydroxylamine hydrochloride (100 g. in 400 ml.) and 3N-sodium hydroxide (48 g.) for 1 hr. After cooling, the deposited oxime recrystallised from benzene (21·4 g., 82%); it had m. p. 100—102° (lit.,[15] for *anti*-isomer 102°) (Found: C, 50·7; H, 3·6; N, 16·6. Calc. for $C_7H_6N_2O_3$: C, 50·6; H, 3·6; N, 16·9%).

o-*Aminobenzaldoxime.*—The above oxime (20 g.) and Adams platinum oxide (320 mg.) in ethanol (220 ml.) was shaken with hydrogen at 713 mm. (absorption 3 mol.). Removal of the catalyst and solvent gave the base which, recrystallised from benzene–light petroleum (b. p. 40—60°), had m. p. 134—135° (lit.,[16] 134—135°) (14·8 g., 90%) (Found: C, 61·8; H, 5·95. Calc. for $C_7H_8N_2O$: C, 61·75; H, 5·9%).

o-*Formamidobenzaldehyde* O-*formyloxime.*—*o*-Aminobenzaldehyde oxime (177 mg.) in an excess of acetic formic anhydride [17] (1·0 ml.) was left at room temperature for 24 hr. Light petroleum (b. p. 40—60°) was added and the *diformyl derivative* filtered off and crystallised from benzene–light petroleum (b. p. 40—60°) (174 mg., 70%), having m. p. 140·5—141·5° (Found: C, 56·3; H, 4·3; N, 14·3. $C_9H_8N_2O_3$ requires C, 56·25; H, 4·2; N, 14·6%).

o-*Acetamidobenzaldoxime.*—*o*-Aminobenzaldehyde oxime (5·4 g., 1 mol.), suspended in dry benzene (50 ml.), was treated with acetic anhydride (4·2 ml., 1·1 mol.) and left at room temperature for 24 hr. Excess of anhydride and benzene was removed *in vacuo*. The residue, crystallised from ethanol, had m. p. 194—195° (lit.,[6] 194°) (5·4 g., 75%) (Found: C, 60·4; H, 5·8; N, 15·6. Calc. for $C_9H_{10}N_2O_2$: C, 60·7; H, 5·7; N, 15·7%).

3,4-*Dihydro*-2-*methylquinazoline.*—(b) *By Bischler's synthesis.* The preceding oxime was reduced with sodium amalgam to the benzylamine and cyclised with anhydrous zinc chloride to the dihydroquinazoline according to Bischler's method.[6] The benzylamine (2 g.) gave 1·06 g. (60%) of the dihydro-compound, b. p. 126°/0·8 mm., 113°/0·2 mm. (lit.,[6] 260—270°/1 atm.). The ultraviolet spectrum at pH 12·3 and 7·0 was identical with that given above and the R_F in solvent (A) was 0·75 and in (B) 0·52. The base gave a hydrochloride, m. p. 285—290° (decomp.) (lit.,[6] no m. p.) with pK_a 10·13 ± 0·05 (M/200) (Found: C, 59·3; H, 6·2; N, 15·2; Cl, 19·5%). The picrate had m. p. 189—190° (lit.,[6] 166—167°) (Found: C, 47·8; H, 3·4%), and under conditions described above it also gave a picrate, m. p. 204—205°.

(c) *Gabriel and Jansen's synthesis.* *o*-Acetamidomethylnitrobenzene (5·55 g.) with 10% palladium–charcoal (1·0 g.) in ethanol (100 ml.) was hydrogenated at 715 mm. The amino-compound, crystallised from benzene–light petroleum (b. p. 40—60°), had m. p. 112—113° (lit.,[4] 112·5—113·5°) (4·2 g., 90%). This base (1·75 g.) was dehydrated by heating at 240° under nitrogen for 6 hr., and the dihydro-compound (1·39 g., 90%) was obtained according to Gabriel and Jansen's method.[4] It had b. p. 112—113°/0·2—0·3 mm. (lit.,[4] 300°/1 atm.), R_F in solvent (A) 0·74 and in (B) 0·53. The ultraviolet spectrum was as above. The hydrochloride had m. p. 288—290° (decomp.) (lit.,[4] 250°) and pK_a 10·06 ± 0·05 (M/200) (Found: C, 59·2; H, 6·0; N, 15·3; Cl, 19·5%), and the picrate m. p. 189—190° (lit.,[4] 180—200°, 185—187°) (Found: C, 48·1; H, 3·4%). This picrate also was dimorphic.

1,4-*Dihydro*-1-*methylquinazoline.*—*o*-Methylaminobenzamide (10 g., 1 mol.) in a Soxhlet apparatus was extracted by boiling ether into a stirred suspension of lithium aluminium hydride (6·1 g., 2·4 mol.) in anhydrous ether (450 ml.) during 6 hr., and the solution was then stirred at room temperature for 12 hr. Excess of the reducing agent was decomposed by water followed by 2N-sodium hydroxide (170 ml.). The aqueous layer extracted with ether (2 × 150 ml.). The combined ethereal solutions were dried (KOH) and evaporated. The residue was triturated with ether and filtered from unchanged amide (2·1 g.). The filtrate was evaporated to dryness, and the residue left in acetic formic anhydride (15 ml.) at room temperature for 48 hr. Excess

[14] Tsang, Wood, and Johnson, *Org. Synth.*, 1944, **24**, 75.
[15] Brady and Dunn, *J.*, 1913, **103**, 1614.
[16] Bamberger and Demuth, *Ber.*, 1901, **34**, 1330.
[17] Béhal, *Compt. rend.*, 1889, **128**, 1460.

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of anhydride was removed *in vacuo* and the residue distilled. The distillate in ethanol (20 ml.) was treated with an excess of picric acid solution, and the *picrate* (3·4 g., 17%) isolated (needles from ethanol; m. p. 176—177°) (Found: C, 48·0; H, 3·6; N, 18·6. $C_{15}H_{13}N_5O_7$ requires C, 48·0; H, 3·5; N, 18·7%). The picrate (3·2 g.) was decomposed with 2·5N-sodium hydroxide (150 ml.), and the base extracted with chloroform (3 × 25 ml.). The extract was dried (Na_2SO_4), the solvent removed *in vacuo*, and the residue distilled (b. p. 90—91°/2·5 mm.). The *methyl derivative* (1·1 g., 91%), a pale yellow, very hygroscopic liquid, was sampled in a dry box (Found: C, 71·7; H, 6·9; N, 18·7. $C_9H_{10}N_2,H_2O$ requires C, 71·7; H, 7·0; N, 18·6%).

N-Benzylisatoic Anhydride.—*N*-Benzylanthranilic acid [18] (34·1 g., 1 mol.) was refluxed with ethyl chloroformate (42·6 ml., 3 mol.) for 15 min. Acetyl chloride (11·5 ml., 1·1 mol.) was then added and the mixture boiled for a further 30 min. On cooling, *N-benzylisatoic anhydride* crystallised; it recrystallised from benzene–light petroleum (b. p. 40—60°) as needles (29·5 g., 78%), m. p. 140—141° (Found: C, 70·9; H, 4·4; N, 5·4. $C_{15}H_{11}NO_3$ requires C, 71·1; H, 4·4; N, 5·5%).

o-*Benzylaminobenzamide.*—The above anhydride (12·6 g.) and ammonia (400 ml.; *d* 0·91) were heated on a steam-bath for 3 hr. with occasional shaking. The *amide* was filtered off and recrystallised from methanol as needles (10·9 g., 96%), m. p. 171—172° (Found: C, 74·1; H, 6·2; N, 12·2. $C_{14}H_{14}N_2O$ requires C, 74·3; H, 6·2; N, 12·4%).

o-*Benzylaminobenzylamine.*—The amide (13·6 g., 1 mol.), in a Soxhlet apparatus, was extracted as above into a suspension of lithium aluminium hydride (10·5 g., 5 mol.) in anhydrous ether (600 ml.) during 10 hr. The mixture was then stirred at room temperature for 20 hr. and worked up as above with 2·5N-sodium hydroxide (375 ml.). The unchanged amide (1·1 g.) was filtered off and the product was passed in benzene through alumina (B.D.H.; 6″ × ¾″). Elution with benzene gave o-*benzylaminobenzylamine* (7·8 g., 61%), needles [from benzene–light petroleum (b. p. 40—60°)], m. p. 50—51°, sublimed at 40—50°/0·2 mm. (Found: C, 78·9; H, 7·7; N, 13·2. $C_{14}H_{16}N_2$ requires C, 79·2; H, 7·6; N, 13·2%).

1-*Benzyl*-1,4-*dihydroquinazoline.*—The preceding amine (3·5 g.) was refluxed in 98—100% formic acid (20 ml.) for ½ hr. The excess of acid was removed *in vacuo* and the residue distilled (b. p. 160—180°/0·6 mm.). The solid distillate of 1-*benzyl*-1,4-*dihydroquinazoline* recrystallised from light petroleum (b. p. 60—80°) as needles (3·2 g., 87%), m. p. 101—102° (Found: C, 80·8; H, 6·3; N, 12·5. $C_{15}H_{14}N_2$ requires C, 81·05; H, 6·35; N, 12·6%). The *picrate*, m. p. 199—200°, crystallised from ethanol (Found: C, 55·65; H, 3·9; N, 15·7. $C_{21}H_{17}N_5O_7$ requires C, 55·9; H, 3·8; N, 15·5%).

This base (222 mg.) in glacial acetic acid (0·6 ml.) was left with a 50% w/v solution of hydrobromic acid in glacial acetic acid (0·6 ml.) at 20—25° for 2 hr. The product, 2-(N-*benzylformamido*)*benzylamine hydrobromide*, recrystallised from methanol as needles (253 mg., 79%), m. p. 224—225° (Found: Br, 25·0; N, 8·7. $C_{15}H_{16}N_2O,HBr$ requires Br, 24·9; N, 8·7%).

Debenzylation of 1-*Benzyl*-1,4-*dihydroquinazoline.*—The dihydro-base (1·11 g., 1 mol.), suspended in liquid ammonia (120 ml.), was treated with sodium (0·46 g., 4 atom-equiv.). After 15 min. the excess of sodium was removed by addition of ammonium chloride and the ammonia evaporated. The residue was extracted with dry benzene (100 ml.), and the solvent removed from the extract *in vacuo*. The residue was distilled (b. p. 134—136°/0·3—0·4 mm.; 446 mg., 69%), and had m. p. and mixed m. p. with 3,4-dihydroquinazoline 125—126° (m. p. and mixed m. p. of the picrates 219—220°) (Found: C, 72·7; H, 6·1; N, 20·9. Calc. for $C_8H_8N_2$: C, 72·7; H, 6·1; N, 21·2%), pK_a 9·21 ± 0·03 (M/200), $\lambda_{max.}$ 221·5, 290 mμ (log ε 4·09, 3·76 in aqueous buffer of pH 12) (cf. ref. 1), and R_F values identical with those of 3,4-dihydroquinazoline in solvents (A) or (B).

Methylation of 3,4-*Dihydroquinazoline.*—The base (1·32 g.) in methanol (10 ml.) was left with methyl iodide (0·62 ml., 1 equiv.) at room temperature. After 48 hr., paper chromatography showed that the reaction was apparently complete and the solid hydriodide had crystallised. The mixture was diluted with water and extracted with benzene. This extract consisted mainly of the starting material, together with a small amount of 3,4-dihydro-3-methylquinazoline as shown by paper chromatography. The aqueous layer was made alkaline and extracted with benzene. The extract was dried (KOH) and evaporated *in vacuo*. The residue solidified and was shown, chromatographically, to consist mainly of 3,4-dihydro-3-methylquinazoline and a trace of the starting material. No 1,4-dihydro-1-methylquinazoline

[18] van Alphen, *Rec. Trav. chim.*, 1942, **61**, 201.

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was detected. The methylation product, purified from benzene–light petroleum (b. p. 40—60°), had m. p. 89—91° (lit.,[19] 90—91°) (0·72 g., 49%). Its picrate had m. p. 197—199° (lit.,[20] 197—199°).

I thank Professor Adrien Albert and Dr. D. J. Brown for most helpful discussion, Mr. F. V. Robinson and Mr. D. T. Light for physical measurements, and Dr. J. E. Fildes and her staff for microanalyses.

DEPARTMENT OF MEDICAL CHEMISTRY, INSTITUTE OF ADVANCED STUDIES,
AUSTRALIAN NATIONAL UNIVERSITY,
CANBERRA, AUSTRALIA. [*Received, November 7th*, 1960.]

[19] Gabriel and Colman, *Ber.*, 1904, **37**, 3642.
[20] Osborn and Schofield, *J.*, 1956, 3977.

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530. β-*Aroylpropionic Acids. Part XX.** *Conversion of* β-(2,5-*Dimethylbenzoyl*)-α- *and* -β-*phenylpropionic Acid into Polynuclear Compounds.*

By F. G. BADDAR, M. F. EL-NEWEIHY, and M. T. EL-ZIMAITY.

The ethoxalyl derivative of ethyl γ-(2,5-dimethylphenyl)-β-phenylbutyrate is cyclised with 80% sulphuric acid, then dehydrogenated to 5,8-dimethyl-3-phenylnaphthalene-1,2-dicarboxylic anhydride. This is cyclised by aluminium chloride in nitrobenzene to 6,9-dimethylbenzo[*b*]fluorenone-10-carboxylic acid. When the ethoxalyl derivative is refluxed with 20% sulphuric acid and then dehydrogenated, it gives rise to 5,8-dimethyl-3-phenyl-1-naphthoic acid. It is decarboxylated to 1,4-dimethyl-6-phenylnaphthalene, identical with the product obtained from γ-(2,5-dimethylphenyl)-α-phenylbutyric acid.

p-XYLENE condensed with phenylsuccinic anhydride in presence of aluminium chloride to give a 2 : 3 mixture of β-(2,5-dimethylbenzoyl)-α- and β-phenylpropionic acid; the higher proportion of the latter acid indicates that non-polar or weakly polar substrates favour the formation of the β-phenyl isomers.[1] The β-phenyl acid was reduced to the butyric acid (Ia), then esterified and condensed with ethyl oxalate in presence of potassium ethoxide,[2] to give the ethoxalyl ester (II) which was cyclised with 80% (v/v) sulphuric acid to the dihydro-anhydride (III). This was dehydrogenated with selenium to the anhydride (IV), then treated with anhydrous aluminium chloride to give 6,9-dimethylbenzo[*b*]fluorenone-10-carboxylic acid (V).

When the crude oxalyl ester (II) was refluxed with 20% (v/v) sulphuric acid,[3] it gave 3,4-dihydro-5,8-dimethyl-3-phenyl-1-naphthoic acid (VI), which was dehydrogenated with selenium to 5,8-dimethyl-3-phenyl-1-naphthoic acid, then decarboxylated to 1,4-dimethyl-6-phenylnaphthalene (VII).

β-(2,5-Dimethylbenzoyl)-α-phenylpropionic acid was reduced by a modified Clemmensen method to γ-(2,5-dimethylphenyl)-α-phenylbutyric acid (VIII), and the crude acid was directly cyclised with phosphorus oxychloride. The product was found to contain 5,8-dimethyl-2-phenyl-1-tetralone (IX), and another ketonic substance, m. p. 89—90°, as the main constituents, with a little 2-phenyl-4-*p*-xylylbut-3-enoic acid lactone. This indicated that the butyric acid was contaminated with unreduced keto-acid. The structure of the tetralone was established by its 2,4-dinitrophenylhydrazone, and its

* Part XIX, *J.*, 1961, 1083.

[1] Cf. Baddar, Fleifel, and Sherif, *J. Chem. U.A.R.*, 1960, **3**, No. 1, 47; Wali, Khalil, Bhatia, and Ahmed, *Proc. Indian Acad. Sci.*, 1941, **14**, *A*, 139.
[2] Baddar, Fleifel, and Sherif, *J.*, 1959, 1009.
[3] Baddar and Warren, *J.*, 1939, 944.

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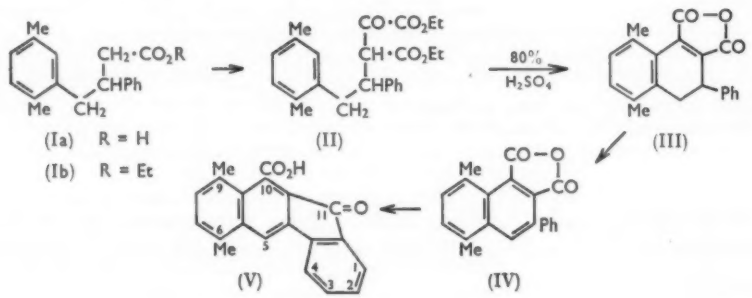
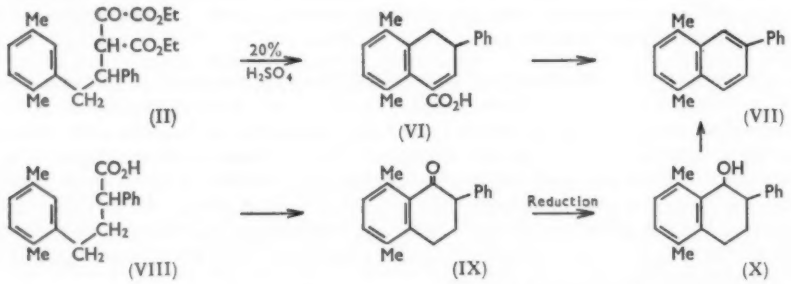
infrared spectrum which showed a strong band at 1670 cm.$^{-1}$, characteristic of αβ-unsaturated six-membered cyclic ketones.[4] The structure of the lactone was established by its identity with a specimen prepared by heating β-(2,5-dimethylbenzoyl)-α-phenylpropionic acid with acetic anhydride; its infrared spectrum showed a band at 1750 cm.$^{-1}$ (KBr disc), characteristic of βγ-unsaturated lactones.[5,6]



The ketonic structure of the product, m. p. 89—90°, was inferred from the formation of a dinitrophenylhydrazone, and the appearance in its infrared spectrum of a strong band at 1680 cm.$^{-1}$ (KBr disc), characteristic of aryl ketones.[7] Its analytical data as well as those of its dinitrophenylhydrazone agree with those calculated for β-phenylpropionyl-*p*-xylene, a product that could have resulted from decarboxylation of β-(2,5-dimethylbenzoyl)-α-phenylpropionic acid. However, the exact structure of this product is still under investigation.



The tetralone (IX) was reduced with lithium aluminium hydride to the tetralol (X), whose infrared spectrum showed a band at 3600 cm.$^{-1}$, characteristic of the unbonded hydroxyl group.[8] Dehydrogenation of the crude tetralol with selenium gave 1,4-dimethyl-6-phenylnaphthalene (VII).

Experimental

Infrared spectra were measured on a Perkin-Elmer Infracord spectrophotometer model 137, for Nujol mulls unless otherwise stated.

β-(2,5-*Dimethylbenzoyl*)-β-*phenylpropionic Acid*.—A stirred ice-cold mixture of phenylacetyl chloride (15·5 g., 1 mol.), *p*-xylene (15 g., 1·5 mol.), and *s*-tetrachloroethane (175 ml.)

[4] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co. Ltd., London, 1956, p. 128.
[5] Baddar and Sherif, *J.*, 1960, 2309.
[6] Ref. 4, p. 153.
[7] Ref. 4, p. 114.
[8] Ref. 4, p. 84.

was treated portionwise with finely powdered aluminium chloride (16 g., 1·2 mol.) at such a rate (0·5 hr.) that the temperature was kept at 0—5°. The mixture was then allowed slowly to attain room temperature and left thereat for 48 hr. with occasional stirring, then poured into ice-cold dilute hydrochloric acid, and the solvent was removed in steam. The oily product (20 g.) was distilled to give 2,5-dimethyldeoxybenzoin, b. p. 182°/5·5 mm. (17 g.). Its oxime, crystallised from dilute ethanol, had m. p. 111—113° (Found: C, 80·6; H, 7·4; N, 5·7. Calc. for $C_{16}H_{17}NO$: C, 80·3; H, 7·2; N, 5·85%). Wege [9] gives m. p. 99°.

2,5-Dimethyldeoxybenzoin (9 g., 1 mol.) was gradually added to potassium ethoxide in absolute ethanol (from potassium, 1·9 g., in absolute ethanol, 30 ml.), and the mixture was refluxed for 4 hr. on a boiling-water bath. Ethyl bromoacetate (6·7 g., 1 mol.) was then added, and refluxing was continued for 10 hr. The mixture was filtered while hot from the precipitated potassium bromide, and the filtrate refluxed for 10 hr. with 7% alcoholic sodium hydroxide (70 ml.) and then poured into ice-cold dilute hydrochloric acid. The product which solidified (1·6 g.) on trituration with light petroleum (b. p. 40—60°) crystallised from ethanol to give β-(2,5-*dimethylbenzoyl*)-β-*phenylpropionic acid*, m. p. 171° (Found: C, 76·25; H, 6·35. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%).

Reaction between p-*Xylene and Phenylsuccinic Anhydride*.—A stirred ice-cold mixture of phenylsuccinic anhydride (17·6 g., 1 mol.), *p*-xylene (21·4 g., 2 mol.), and *s*-tetrachloroethane (300 ml.) was treated portionwise with finely powdered aluminium chloride (33·6., 2·5 mol.) at such a rate that the temperature was kept at 0—5° during the addition (½ hr.). Then the mixture was allowed slowly to attain room temperature, left thereat for 48 hr. with occasional stirring, and worked up as usual.[5] The crude acid (27 g.) had m. p. 140—169°, shrinking at 145°, indicating that it was a mixture. On crystallisation from ethanol β-(2,5-dimethylbenzoyl)-β-phenylpropionic acid (15·5 g.), m. p. and mixed m. p. 171°, was obtained (Found: C, 77·1; H, 6·3. Calc. for $C_{18}H_{18}O_3$: C, 76·6; H, 6·4%); its infrared spectrum showed two strong bands at 1724 and 1680 $cm.^{-1}$. The mother-liquor was evaporated to dryness and the residue crystallised from benzene–light petroleum (b. p. 40—60°) to give β-(2,5-*dimethylbenzoyl*)-α-*phenylpropionic acid* (10 g.), m. p. 130° (Found: C, 76·7; H, 6·4%).

γ-(2,5-*Dimethylphenyl*)-β-*phenylbutyric Acid* (Ia).—A solution of β-(2,5-dimethylbenzoyl)-β-phenylpropionic acid (12 g.) in pure sulphur-free toluene (200 ml.) was refluxed with amalgamated zinc (B.D.H.) (150 g.), concentrated hydrochloric acid (200 ml.), and water (50 ml.), for 150 hr., during which further zinc (100 g.), concentrated hydrochloric acid (200 ml.), and water (50 ml.) were added portionwise. The mixture was filtered, and the toluene layer was extracted with 10% sodium hydroxide solution. The oily acid precipitated on acidification crystallised from light petroleum (b. p. 40—60°), to give γ-(2,5-*dimethylphenyl*)-β-*phenylbutyric acid* (8 g.), m. p. 92—93 (Found: C, 80·0; H, 7·3. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·5%).

The *ethyl ester* (prepared by means of ethyl alcohol–hydrogen chloride) had b. p. 171°/0·1 mm. (Found: C, 81·2; H, 8·1. $C_{20}H_{24}O_2$ requires C, 81·1; H, 8·1%).

3,4-*Dihydro*-5,8-*dimethyl*-3-*phenylnaphthalene*-1,2-*dicarboxylic Anhydride* (III).—Pure powdered potassium (1·6 g., 1 mol.) was covered with dry ether (100 ml.), stirred, and treated portionwise with absolute ethanol (*ca.* 4 ml.). When the evolution of hydrogen ceased, ethyl oxalate (8·8 g.; 1·5 mol.) was added, and the light yellow solution was left for 1 hr. Ethyl γ-(2,5-dimethylphenyl)-β-phenylbutyrate (11·4 g., 1 mol.) was next added and the wine-red solution was left overnight, then gently heated on a boiling-water bath for 7 hr., poured into ice-cold dilute sulphuric acid, and worked up as usual.[2] The crude oxalyl ester (19·2 g.) was directly used in the following experiment.

It was stirred on a boiling-water bath with 80% (v/v) sulphuric acid (150 ml.) for 1 hr. The mixture was poured on ice, and the precipitated viscous brown oil (10 g.) was boiled with sodium carbonate solution, filtered, cooled, and acidified. The precipitated semisolid dibasic acid (7·2 g.) was refluxed with acetyl chloride, which upon evaporation left a solid (3·8 g.). On crystallisation from light petroleum (b. p. 60—80°) greenish-yellow 3,4-*dihydro*-5,8-*dimethyl*-3-*phenylnaphthalene*-1,2-*dicarboxylic anhydride* was obtained having m. p. 130—132° (Found: C, 79·4; H, 5·5. $C_{20}H_{16}O_3$ requires C, 78·95; H, 5·3%).

5,8-*Dimethyl*-3-*phenylnaphthalene*-1,2-*dicarboxylic Anhydride* (IV).—A powdered mixture of the preceding anhydride (1·1 g.) and selenium (0·9 g.) was heated at 290° for 8 hr., cooled, and then extracted with boiling benzene. The product (0·7 g.) that crystallised on cooling

[9] Wege, *Ber.*, 1891, **24**, 3540.

recrystallised from benzene–light petroleum (b. p. 40—60°) to give 5,8-*dimethyl*-3-*phenylnaphthalene*-1,2-*dicarboxylic anhydride* in yellow needles, m. p. 210° (Found: C, 79·0; H, 4·5. $C_{20}H_{14}O_3$ requires C, 79·5; H, 4·6%).

6,9-*Dimethylbenzo*[b]*fluorenone*-10-*carboxylic Acid* (V).—Nitrobenzene (10 ml.) was cooled with stirring to 10°, then treated portionwise with a mixture of the preceding anhydride (0·5 g., 1 mol.) and aluminium chloride (*ca.* 1 g., 4 mol.) during 1 hr. The mixture was kept at 10° for 2 hr., then left at 55—60° for ½ hr. and overnight at room temperature, and was worked up as usual.[9] The precipitated *acid* crystallised from acetic acid in yellow needles (0·3 g.), m. p. >300° (Found: C, 78·5; H, 4·6. $C_{20}H_{14}O_3$ requires C, 79·5; H, 4·6%).

3,4-*Dihydro*-5,8-*dimethyl*-3-*phenyl*-1-*naphthoic Acid* (VI).—The crude oxalyl ester (II) (16·7 g.) was refluxed with 20% (v/v) sulphuric acid (170 ml.) for 56 hr., then worked up as usual.[9] The product (6 g.), which partially solidified during 1 month, crystallised from dilute ethanol to give 3,4-*dihydro*-5,8-*dimethyl*-3-*phenyl*-1-*naphthoic acid*, m. p. 165° (Found: C, 82·3; H, 6·7. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5%).

5,8-*Dimethyl*-2-*phenyl*-1-*tetralone* (IX).—(i) *Reduction of the* α-*phenyl-keto-acid.* A mixture of β-(2,5-dimethylbenzoyl)-α-phenylpropionic acid (15 g.), toluene (sulphur-free; 200 ml.), zinc amalgam (250 g.) (B.D.H), concentrated hydrochloric acid (200 ml.), and water (75 ml.) was refluxed for 90 hr., during which further concentrated hydrochloric acid (100 ml.) was added portionwise. The mixture was worked up as in the analogous experiment above. The viscous yellow oil (12·7 g.) was used directly in the following step.

(ii) *Cyclisation of the butyric acid.* Phosphorus oxychloride (30 ml.) was gradually added to a boiling solution of the crude butyric acid (24·5 g.) in dry *s*-tetrachloroethane (350 ml.); the mixture was gently refluxed for 2·5 hr., during which a semisolid product separated. The mixture was poured into ice-cold water, and the solvent removed with steam. The dark brown oily product (19·7 g.) was distilled, to give three fractions. (*a*) A *substance*, b. p. 240°/0·2 mm., solidified (7·6 g.) on trituration with light petroleum (b. p. 40—60°) and had m. p. 89—90° (from dilute ethanol) (Found: C, 85·3; H, 7·3. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%). Its red 2,4-*dinitrophenylhydrazone* had m. p. 200° (from ethanol) (Found: C, 66·8; H, 5·1; N, 13·1. $C_{23}H_{22}N_4O_4$ requires C, 66·0; H, 5·3; N, 13·4%). (*b*) A second fraction, b. p. 280°/0·2 mm., on treatment with light petroleum (b. p. 40—60°), gave 2-*phenyl*-4-p-*xylylbut*-3-*enoic acid lactone* (0·55 g.) which, crystallised from light petroleum (b. p. 60—80°), had m. p. 127—128° (Found: C, 81·7; H, 6·2. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%); it was identified by mixed m. p. with a specimen, m. p. 127—128°, prepared by heating β-(2,5-dimethylbenzoyl)-α-phenylpropionic acid with acetic anhydride.[10] (*c*) The light-petroleum washings from (*a*) and (*b*) gave on evaporation a viscous oil (7·5 g.), which was identified as 5,8-dimethyl-2-phenyl-1-tetralone through its 2,4-*dinitrophenylhydrazone*, red crystals (from ethyl acetate), m. p. 242° (Found: C, 66·9; H, 5·2; N, 12·9. $C_{24}H_{22}N_4O_4$ requires C, 67·0; H, 5·1; N, 13·0%). The infrared spectrum of the tetralone showed two bands at 1670 and 1750 cm.$^{-1}$; the latter band which is probably due to contamination with the above lactone disappeared in the spectrum of the dinitrophenylhydrazone (KBr disc).

1,4-*Dimethyl*-6-*phenylnaphthalene* (VII).—(i) A solution of the preceding tetralone (2·8 g.) in dry ether (90 ml.) was added during ½ hr. to a suspension of lithium aluminium hydride (1·8 g., excess) in dry ether (90 ml.). The mixture was refluxed for 3 hr., left overnight, and worked up as usual. The product was distilled, to give the tetralol (X), b. p. 250°/0·2 mm. (2·5 g.), $\nu_{max.}$ 3600 cm.$^{-1}$. It was used directly in the following step.

The tetralol (1 g.) was heated with selenium powder (1 g.) at 230° for 8 hr. The mixture was extracted with ether, and a solution of the product in light petroleum (b. p. 40—60°) was left to evaporate slowly at room temperature. The precipitated solid (0·5 g.) crystallised from methanol (3 days at 0°), to give 1,4-*dimethyl*-6-*phenylnaphthalene*, m. p. 70° (Found: C, 92·3; H, 6·9. $C_{18}H_{16}$ requires C, 93·05; H, 6·95%).

(ii) A mixture of 3,4-dihydro-5,8-dimethyl-3-phenyl-1-naphthoic acid (1·2 g.) and selenium (0·6 g.) was heated at 240° for 8 hr. The product was extracted with boiling benzene, the solvent was then evaporated, and the residue was extracted with boiling sodium carbonate solution. The oily acid (0·7 g.) precipitated on acidification was distilled in a vacuum, to give 5,8-dimethyl-3-phenyl-1-naphthoic acid, b. p. 260°/0·5 mm., which solidified on long storage. To a stirred mixture of this acid (0·5 g.) and quinoline (5 ml.), copper bronze (*ca.* 0·1 g.) was

[10] Kugel, *Annalen*, 1898, **299**, 54.

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added portionwise while the mixture was gradually heated on a sand-bath. The mixture was refluxed for 1 hr., then worked up as usual. The product crystallised from methanol (2 days at 0°), to give 1,4-dimethyl-6-phenylnaphthalene, m. p. 70°, undepressed on admixture with the specimen prepared by method (i).

A'IN SHAMS UNIVERSITY, FACULTY OF SCIENCE,
CAIRO, U.A.R.

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531. *Tetrahedral Nickel*(II) *Complexes and the Factors Determining Their Formation. Part II.* Complexes with Dibutylphenylphosphine and Butyldiphenylphosphine.*

By C. R. C. COUSSMAKER, M. HELY HUTCHINSON, J. R. MELLOR, L. E. SUTTON, and L. M. VENANZI.

The preparation and properties of some complexes of the type L_2NiX_2 ($L = Bu^n_2PhP$ or Bu^nPh_2P; X = Cl, Br, I, SCN, or NO_3) are reported. The complexes where $L = Bu^n_2PhP$ and X = Cl, Br, or I are diamagnetic and have been assigned a *trans*-planar structure. The corresponding derivatives of Bu^nPh_2P are paramagnetic and presumably tetrahedral in the solid state, while in benzene solution they appear to form mixtures of diamagnetic and paramagnetic forms. The changes of magnetic susceptibility with changes of phosphine are discussed.

THE co-ordination compounds of nickel(II) halides with trialkylphosphines have a *trans*-planar structure,[1,2] whereas those with triphenylphosphine have a tetrahedral structure.[3] Also, the complexes of trialkylphosphines are diamagnetic while those of triphenylphosphine have magnetic susceptibilities indicating the presence of two unpaired electrons, as reported in Part I.* We now report the structural and magnetic changes as a function of the number of phenyl groups attached to the phosphorus atom.

TABLE 1. *Colour, decomposition point, electric dipole moment, and magnetic moment of phosphine complexes of nickel*(II).

Compound	Colour	Decomp. pt.	μ (D)	$\mu_{eff.}$ (B.M.) *
$(Et_3P)_2Ni(SCN)_2$	Yellow	141—142°	—	Diamag.
$(Bu^n_2PhP)_2NiCl_2$	Red	56—57	1·3	Diamag.
$(Bu^n_2PhP)_2NiBr_2$	Dark red	70—71	1·9	Diamag.
$(Bu^n_2PhP)_2NiI_2$	Bronze	87—88	3·1	Diamag.
$(Bu^n_2PhP)_2Ni(NO_3)_2$	Green	98—99	9·8	3·16
$(Bu^n_2PhP)_2Ni(SCN)_2$	Orange	120—121	1·8	Diamag.
$(Bu^nPh_2P)_2NiCl_2$	Blue	149—150	3·3	3·35
$(Bu^nPh_2P)_2NiBr_2$	Green	161—162	5·9	3·30
$(Bu^nPh_2P)_2NiI_2$	Brown	134—135	6·8	3·18
$(Bu^nPh_2P)_2Ni(NO_3)_2$	Green	154—155	9·8	3·40
$(Bu^nPh_2P)_2Ni(SCN)_2$	Orange	144—145	2·0	Diamag.
$\{(Cl{\cdot}CH_2)_3P\}_2NiBr_2$	Deep red	158—159	1·5	Diamag.
$\{(Cl{\cdot}CH_2)_3P\}_2NiI_2$	Brown-black	125—126	—	Diamag.

* In the solid state.

A number of dialkylarylphosphine and diarylalkylphosphine complexes of nickel(II) have been reported but they have not been fully investigated.[1,4,5] Two main series of complexes are described in the present paper: those of dibutylphenylphosphine and those

* Part I, *J.*, 1958, 719.

[1] Jensen, *Z. anorg. Chem.*, 1936, **229**, 265.
[2] Asmussen, *Acta Chem. Scand.*, 1955, **9** 1391; Scatturin, *J. Inorg. Nuclear Chem.*, 1958, **8**, 447.
[3] Henn, Garton, Powell, and Venanzi, unpublished work.
[4] Cass, Coates, and Hayter, *J.*, 1955, 4007.
[5] Chatt and Shaw, *J.*, 1960, 1718.

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of butyldiphenylphosphine with nickel chloride, bromide, iodide, nitrate, and thiocyanate. They were prepared by adding the liquid ligand, in a nitrogen atmosphere, to a solution of nickel salt in butan-1-ol (or ethanol in the case of nickel chloride, which is insoluble in

TABLE 2. *Temperature-dependence of paramagnetic polarisations.*

Complex	$10^6\chi_M$ (uncorr.)	$10^6\chi_M$ (corr.)	Temp. (K)	$\mu_{eff.}$ (B.M.)
$(Bu_3PhP)_2NiCl_2$	−299	+95·0 *	287°	—
$(Bu_3PhP)_2NiBr_2$	−302	+112 *	287	—
$(Bu_3PhP)_2NiI_2$	−314	+132	287	—
$(Bu_3PhP)_2Ni(SCN)_2$	−402	+10·2	290	—
$(BuPh_2P)_2NiCl_2$	+4439	+4829	288	3·35
	+5877	+6265	217	
	+7640	+8028	171	
$(BuPh_2P)_2NiBr_2$	+4095	+4507	290	3·30
	+5390	+5794	223	
	+7082	+7489	171	
$(BuPh_2P)_2NiI_2$	+3914	+4350	289	3·18
	+5130	+5570	219	
	+7036	+7475	161	
$(BuPh_2P)_2Ni(SCN)_2$	−326	+78·7	290	—

* Measurements with these compounds were also carried out at lower temperatures; the value for the corrected molar susceptibility was constant in each case.

TABLE 3. *Absorption spectra* (λ *in* mμ).

Complex	Solution $\lambda_{max.}$	Solution ε	Solid $\lambda_{max.}$	Solid "Absorbency" *D*
$(Et_3P)_2NiCl_2$	370	14,200		
	490	450		
$(Et_3P)_2NiBr_2$	400	6200		
	542	350		
$(Et_3P)_2NiI_2$	373	4690		
	459	2900		
	610	485		
$(Bu_3PhP)_2NiCl_2$	379	11,680	360	1·48
	495	670	390—425	sh
			500	1·29
$(Bu_3PhP)_2NiBr_2$	405	8500	385	1·67
	540	576	425—450	sh
			510	1·335
$(Bu_3PhP)_2NiI_2$	370	4040	440	1·595
	463	2750	500—575	sh
	600	490	650—725	sh
			490—510	1·58
$(BuPh_2P)_2NiCl_2$	386	4560	390	1·556
	495	692	560—580	1·30
	875	35·2	900	1·245
$(BuPh_2P)_2NiBr_2$	413	5660	420	1·54
	550	476	560—580	1·30
	880	117	912	1·135
$(BuPh_2P)_2NiI_2$	320	4530	430—450	1·60
	400	3460	500—575	sh
	500—600	sh	650—750	sh
	925	374	940	1·485
$(Et_3P)_2Ni(SCN)_2$	370	11,000	340	1·295
	450—525	sh	460	1·25
$(Bu_3PhP)_2Ni(SCN)_2$	388	9550	360	1·47
	475—525	sh	450—500	sh
$(BuPh_2P)_2Ni(SCN)_2$	402	8930	380	1·50
	475—550	sh	475—525	sh

butanol). The complexes separated immediately or in a few minutes. Those which were characterized are listed in Table 1, with their properties. All of them are non-electrolytes in nitrobenzene solution.

Complexes of Dibutylphenylphosphine.—These follow closely the pattern observed for the trialkylphosphine complexes. The halides and the thiocyanate are diamagnetic and monomeric. Measurements of electric dipole moments show that they are essentially *trans*-planar in solution. The observed finite moments could be attributed to small amounts of the *cis*-isomer present in solution. Small amounts of free ligand are known to catalyse *cis–trans*-equilibration of this type,[6] and our complexes, being fairly labile, are very likely to contain small amounts of free phosphine.

It is interesting that for these complexes, after correction for the diamagnetic contribution of the component atoms, there is a small residual paramagnetic polarization

FIG. 1. *Spectra of* $(Bu^n_2PhP)NiX_2$ *in benzene.*

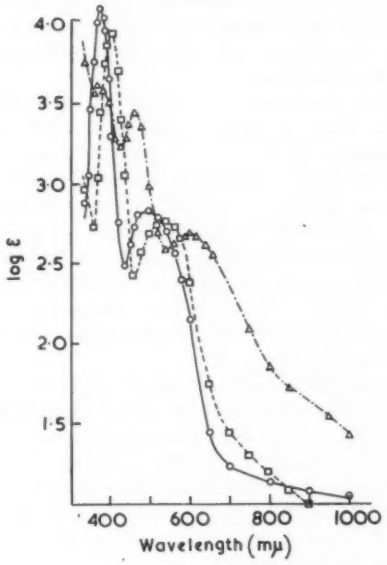
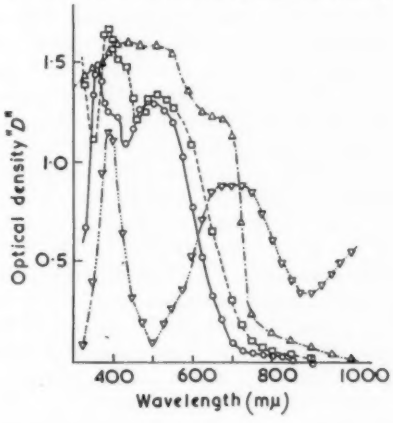


FIG. 2. *Reflection spectra of* $(Bu^n_2PhP)NiX_2$.



○–○ X = Cl. □–□ X = Br. △–△ X = I.
▽–▽ *Reflection spectrum of* $NiSO_4,7H_2O$.

which, at least in $(Bu^n_2PhP)_2NiCl_2$ and $(Bu^n_2PhP)_2NiBr_2$, appears to be temperature-independent (see Table 2). The only paramagnetic complex isolated is the nitrato-derivative. Its structure, like that of its triethylphosphine analogue, is still unknown.

The absorption spectra in the region 375—1000 mμ for the complexes of dibutylphenylphosphine in benzene solution are reproduced in Fig. 1. They are closely similar to those of the corresponding complexes of triethylphosphine (see Table 3). Essentially they consist of: (1) a very intense absorption band at about 400 mμ, which has been assigned to 3*d*–4*p* transitions [7] (iodo-complexes show two bands of high frequency and high intensity) and (2) the crystal-field bands in the region 500—600 mμ, which are not resolved. Our spectra are similar to those found by Giacometti and Turco [8] for other trialkylphosphine derivatives of nickel(II).

[6] Chatt and Wilkins, *J.*, 1956, 525, and references quoted there.
[7] Williams, *J.*, 1955, 137; Orgel, *J. Chem. Phys.*, 1955, **23**, 1004.
[8] Giacometti and Turco, *J. Inorg. Nuclear Chem.*, 1960, **15**, 242.

Attempts were made to see whether shifts of the crystal-field bands occurred on changing from benzene to a donor solvent, as observed by Chatt *et al.*[9] for complexes of platinum(II). As our complexes were decomposed by alcohols (at a rate decreasing with increasing length of the alkyl chain of the alcohol), acetone was used: there was a slight decrease in intensity of the crystal-field bands, but no band shifts could be observed.

The reflection spectra of the solid complexes of the dialkylaryl derivatives in the region 375—1000 mμ were also recorded and these are shown in Fig. 2. The intensities are plotted on an arbitrary absorbency scale. The reflection spectrum of nickel sulphate heptahydrate, measured under similar experimental conditions, is plotted on the same graph. Our spectrum of this hydrate agrees with that reported elsewhere.[10] The major changes in spectra on passing from solution to the solid state are (1) broadening of the crystal-field bands, (2) striking decrease in intensity of the 400 mμ bands, (3) splitting of the short-wavelength bands, and (4) almost complete lack of resolution of the spectrum in the iodide complexes. There is, however, no apparent shift in the maxima of the absorption bands.

Thus, our results show that the complexes of nickel(II) with dibutylphenylphosphine are, in all respects, analogous to those with trialkylphosphines.

Complexes of Butyldiphenylphosphine.—These complexes, in contrast with those of dibutylphenylphosphine, resemble very closely those of triphenylphosphine: the only diamagnetic complex is that with nickel thiocyanate, all the others being paramagnetic in the solid state, with magnetic moments of 3·2—3·4 B.M. The temperature-dependence of the magnetic susceptibility of the solid complexes appears to follow the Curie–Weiss law over the range of temperatures investigated (160—290° K) (see Table 2). The three halogeno-complexes of this series and the thiocyanate derivative are monomeric in benzene solution, but the nitrato-complex is not sufficiently soluble in non-donor solvents to allow molecular-weight determination. The values of the electric dipole moments of the halogeno-complexes fall between those of the corresponding dibutylphenylphosphine and triphenylphosphine analogues (see Table 1 and Part I).

The visible and ultraviolet spectra of the complexes with butyldiphenylphosphine in benzene solution differ from those with dibutylphenylphosphine, the major change being the appearance of a new band at about 875—925 mμ (Fig. 3). The reflection spectra of the complexes of this series, moreover, differ from those of benzene solutions (Fig. 4): all the bands are shifted towards longer wavelengths, the crystal-field band by as much as 75 mμ. The long-wavelength bands are absent for the diamagnetic complexes of dibutylphenylphosphine, but are observed in the reflection spectra of complexes of the type $(Ph_3P)_2NiX_2$ which have tetrahedral structure in the solid state.[11]

Measurements of magnetic susceptibility of benzene solutions of the butyldiphenylphosphine halide complexes of nickel(II) were carried out by Mills and Williams,[12] who found them to have magnetic moments lower than expected for the presence of two unpaired electrons. If it is assumed that these intermediate values are due to the equilibrium:

$$(BuPh_2P)_2NiX_2 \rightleftharpoons (BuPh_2P)_2NiX_2$$
Diamagnetic Paramagnetic ($\mu_{eff.} = 3{\cdot}2$ B.M.)

then the amounts of the paramagnetic form present in solution can be calculated. Thus one obtains the following approximate percentages of diamagnetic form: $(BuPh_2P)_2NiCl_2$ 10%; $(BuPh_2P)_2NiBr_2$ 60%; and $(BuPh_2P)_2NiI_2$ 90%.

Two hypotheses can be put forward to explain this behaviour: (1) The diamagnetic and the paramagnetic species of the halogeno-complexes of butyldiphenylphosphine have

[9] Chatt, Gamlen, and Orgel, *J.*, 1958, 486; 1959, 1047.
[10] Bostrup and Jörgensen, *Acta Chem. Scand.*, 1957, **11**, 1223.
[11] Davies and Venanzi, unpublished observations.
[12] Mills and Williams, personal communication.

the same structure in benzene solution. To account for the high dipole moments one has then to assume that the complexes are either *cis*-planar or distorted tetrahedral. The magnetic susceptibility of the benzene solutions could then be accounted for in terms of a diamagnetic ground state with an easily accessible paramagnetic excited state, with a multiplet separation of less than kT. (2) In benzene solution an equilibrium is set up between a *trans*-planar diamagnetic form and a tetrahedral (or *cis*-planar) paramagnetic form. Available data do not allow a definite choice but in our opinion the former is more likely.

All the thiocyanate complexes are diamagnetic and their low electric dipole moments

FIG. 3. *Spectra of* $(Bu^nPh_2P)NiX_2$ *in benzene.*

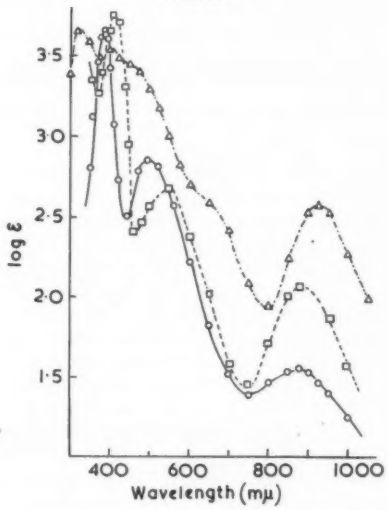
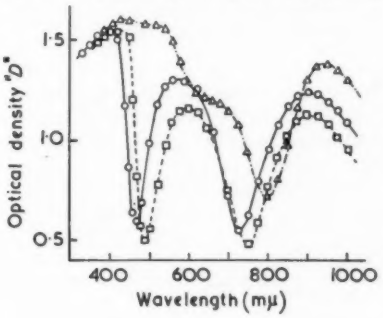


FIG. 4. *Reflection spectra of* $(Bu^nPh_2P)NiX_2$.



○–○ X = Cl. □–□ X = Br. △–△ X = I.

indicate a *trans*-planar structure. In general, thiocyanates give rise to crystal field splittings larger than those due to the chloride ion,[13] and our spectral measurements are in agreement with this (see Table 3). That thiocyanate complexes of the type $(R_3P)_2Ni(SCN)_2$ are diamagnetic, irrespectively of the nature of the phosphine, may therefore be attributed to the increased crystal-field splitting induced by the thiocyanate ion.

The contribution of the phosphines to the crystal-field splitting was shown by the thiocyanate complexes, which are the only set of compounds that is planar and diamagnetic throughout. The bands in question appear only as a shoulder at about 500 mμ, both in benzene solutions and in the solid state (see Table 3). The shifts are slight but they are towards longer wavelengths on going from Et_3P to $Bu^n{}_2PhP$ to Bu^nPh_2P, which indicates that the field becomes weaker on replacement of alkyl by phenyl groups.

For our discussion it will be assumed that the splitting between the *d*-energy levels in the square-planar complexes of nickel(II) is similar to that postulated by Chatt and Shaw [5] (see Fig. 5*b*). The spin multiplicity will be assumed to depend on the energy difference Δ between the $d_{x^2-y^2}$ and the d_{xy} energy level. If the energy difference Δ falls below a certain critical value, the increased crystal-field energy of the low-spin complex over the high-spin one may be insufficient to compensate for the loss of exchange energy which accompanies

[13] See Mitchell and Williams, *J.*, 1960, 1912.

spin-pairing, and a paramagnetic complex will result. One could envisage this complex as preserving the square planar structure, in which the crystal-field energy might be quite small and not significantly different from that of the corresponding tetrahedral complex.[14] In the solid state the configuration of the complex will then be determined by the lattice energy, *i.e.*, by the ease of packing of the monomeric units in the unit cell. For our paramagnetic complexes the tetrahedral configuration appears to be preferred and " frozen " in the crystal lattice. In solution, however, steric repulsions between the ligands could lead to a highly distorted tetrahedral structure, with the small multiplet separation mentioned earlier.

Evidence for this hypothesis is supplied by the spectra of the halogeno-complexes of butyldiphenylphosphine both in the solid state and in solution. As mentioned earlier, the crystal-field bands are shifted by about 75 mμ towards shorter wavelength on going from the solid state to the solution (compare Figs. 3 and 4).

FIG. 5. *Proposed energy level diagram in complexes of the type* L_2NiX_2.

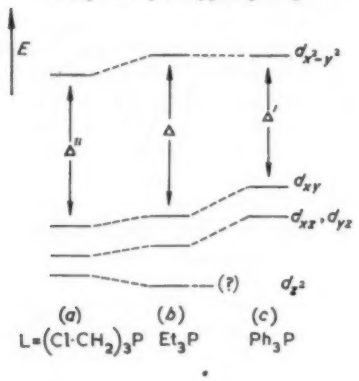
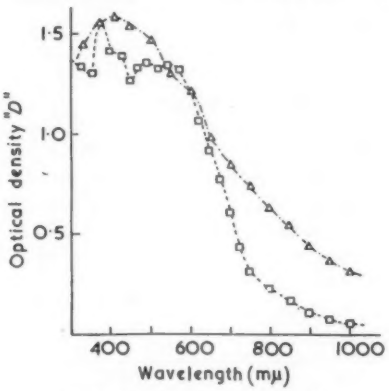


FIG. 6. *Reflection spectra of* $\{(Cl\cdot CH_2)_3P\}_2NiX_2$.



□–□ X = Br. △–△ X = I.

The gradual replacement of alkyl by phenyl groups at the phosphorus atom might be expected to weaken the crystal field generated by the ligand in two ways: (1) Inductively, by increasing the difference in electronegativity between the donor atom and the substituents. This would result in a decreased electron-donor capacity of the phosphorus atom, and consequent decrease in field strength.

(2) Mesomerically, by overlap of the π-aromatic electrons of the benzene ring (or rings) with the 3*d*-orbitals of the phosphorus atom, and consequent decrease of the π-acceptor capacity of the phosphorus atom. This, in turn, would reduce the splitting of energy levels, particularly the critical splitting of the two uppermost levels, upon which depend the magnetic properties of the complex. This relation is illustrated diagrammatically in Fig. 5c.

In an attempt to gauge the relative importance of these two factors in causing the observed structural and magnetic changes, complexes of trischloromethylphosphine, $(Cl\cdot CH_2)_3P$, were studied. Only the bromo- and iodo-complexes are reported here, as we failed to prepare the corresponding chloro-, thiocyanato-, and nitrato-derivatives. The complexes of this series are diamagnetic in the solid state. The spectra in solution could not be obtained because the compounds were either insoluble in, or decomposed by, solvents suitable for such a study. The spectra of the solids are given in Fig. 6.

[14] Maki, *J. Chem. Phys.*, 1958, **28**, 651.

It is interesting that the crystal-field bands in these complexes occur at approximately the same wavelength as in the corresponding triethylphosphine complexes.

The inductive effect of the phenyl and chloromethyl groups can be estimated from the K_a values of phenylacetic and β-chloropropionic acid, which are $4{\cdot}88 \times 10^{-5}$ and $8{\cdot}2 \times 10^{-5}$ respectively.[15] Thus the chloromethyl group is slightly more electron-attracting (electronegative) than the phenyl group and ought therefore to decrease the crystal-field strength more than the latter group does. It follows then, on our hypothesis, that, if a change of electronegativity of the substituent at the phosphorus atom were the main factor causing the observed changes, the trischloromethylphosphine complexes should be paramagnetic, like their phenyl analogues. That this is not the case indicates that, at least in the complexes of nickel(II), d_π–d_π bonding between nickel and phosphorus is important in determining the magnetic susceptibility of the complexes, because this π-bonding appears to be significantly weakened by mesomeric interaction between the aromatic hydrocarbon radical and the phosphorus atom. The absence of such mesomeric interaction in the complexes of trischloromethylphosphine must be responsible for the diamagnetism of its nickel(II) complexes, as the electron-attracting power of the chloromethyl group would render the phosphine a poor σ-electron donor (see Fig. 5*a*).

Experimental

Preparation of Phosphines.—Dibutylphenylphosphine was prepared by the method of Davies and Jones [16] from dichlorophenylphosphine and butylmagnesium bromide. Butyldiphenylphosphine was prepared from butyldichlorophosphine [17] and phenylmagnesium bromide, and from chlorodiphenylphosphine and butylmagnesium bromide, the experimental conditions being similar to those used by Davies and Jones. The fraction of b. p. 120—150°/1 mm. was collected (*ca.* 70% yield) and used for the preparation of the complexes. Trischloromethylphosphine was prepared from tetrakishydroxymethylphosphonium chloride by Hoffman's method.[18] Tetrakischloromethylphosphonium chloride was recrystallized from methanol (30 c.c.) and ethyl acetate (160 c.c.), and melted at 202—203° (Hoffman gives 192—193°); when the phosphine was extracted with ether the yield was the same.

Although described as a colourless stable liquid by Hoffman, the phosphine was found to become cloudy within a few hours of preparation: this occurred on each of the four occasions on which it was prepared, despite the most rigid precautions to exclude oxygen on one occasion. Freshly prepared phosphine was used in the preparation of the complexes.

Preparations of the Complexes.—These were prepared by adding the phosphine (slightly >2 equiv.) to a solution of the nickel salt in an alcohol. Nickel chloride hexahydrate was dissolved in ethanol, and nickel bromide trihydrate and nickel nitrate hexahydrate in butan-1-ol. The solution of nickel iodide (or thiocyanate) was prepared by dissolving the stoicheiometric amount of sodium iodide (or potassium thiocyanate) in boiling butan-1-ol and adding it to a solution of nickel nitrate in butan-1-ol, filtering off the precipitate, and using the solution directly.

All preparations of the complexes were under nitrogen. In each case the complexes gradually crystallized and the mixture was cooled in ice-water before collection of the product.

The solvent used for recrystallization of the crude product, the yield of pure product, and the analytical results are tabulated for each *compound* prepared.

Analytical.—Some of the nickel analyses were carried out gravimetrically with dimethylglyoxime, and some spectrophotometrically, by measuring the absorbence of solutions of the complex produced by oxidation of bis(dimethylglyoxime)nickel(II) in the absence of ammonia.[19] The ashing of the samples before the nickel determination was done with equal volumes of concentrated nitric acid and 72% perchloric acid, refluxing for ~6 hr.

Determination of Molecular Weights.—In a previous communication it was reported that the halogeno-complexes of butyldiphenylphosphine were dimeric.[20] Subsequent investigations

[15] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 733 *et seq.*
[16] Davies and Jones, *J.*, 1929, 33.
[17] Fox, *J. Amer. Chem. Soc.*, 1950, **72**, 4147.
[18] Hoffman, *J. Amer. Chem. Soc.*, 1930, **52**, 2995.
[19] Sandell, "Colorimetric Determination of Traces of Metals," 3rd edn., Interscience, Publ. Inc., New York, 1959, p. 668.
[20] Coussmaker, Hely-Hutchinson, Sutton, and Venanzi, International Conference on Co-ordination Compounds, London, April 6—11th, 1959; *Chem. Soc. Special Publ.* No. 13, p. 160.

Complexes, $(Phosphine)_2NiX_2$.

Phosphine	X	Cryst. from [a]	Yield (%)	Found Ni (%)	Found *M*	Formula	Required Ni (%)	Required *M*
PEt_2	SCN	Me·NO_2	54	14·2	—	$C_{14}H_{30}N_2NiP_2S$	14·3	—
$PPhBu^n_2$	Cl	EtOH	61	10·2	570	$C_{28}H_{46}Cl_2NiP_2$	10·2	574
,,	Br	,,	53	8·9	630	$C_{28}H_{46}Br_2NiP_2$	8·85	663
,,	I	,,	62	7·8	750	$C_{28}H_{46}I_2NiP_2$	7·75	757
,,	NO_3	EtOAc–Pet	55	9·2	680	$C_{28}H_{46}N_2NiO_6P_2$	9·4	627
,,	SCN	EtOH	30	9·5	580	$C_{30}H_{46}N_2NiP_2S_2$	9·5	620
PPh_2Bu^n	Cl	Me·NO_2	53	9·7	[b]	$C_{32}H_{38}Cl_2NiP_2$	9·6	614
,,	Br	,,	60	8·4	[c]	$C_{32}H_{38}Br_2NiP_2$	8·35	703
,,	I	,,	32	7·5	[d]	$C_{32}H_{38}I_2NiP_2$	7·4	797
,,	NO_3	,,	27	8·9	710	$C_{32}H_{38}N_2NiO_6P_2$	8·8	660
,,	SCN	,,	54	8·8	—	$C_{34}H_{38}N_2NiP_2S_2$	8·9	—
$P(CH_2Cl)_3$	Br	[e]	42	10·2	—	$C_6H_{12}Br_2Cl_6NiP_2$	10·2	—
,,	I	[e]	54	8·5	—	$C_6H_{12}Cl_6I_2NiP_2$	8·7	—

[a] Pet = light petroleum (b. p. 40—60°). [b] 600, 589, 472. [c] 570, 648, 728, 692, 708, 690, 619. [d] 666, 781. [e] Crystallised (pure) on partial evaporation of the reaction mixture.

showed that all the complexes listed in Table 1 for which such measurements could be carried out were monomeric. These measurements were carried out cryoscopically in benzene.

Conductance Measurements.—These were done with a 10^{-3}M-solution of the complex in nitrobenzene, a Type E 7566 Mullard conductivity bridge being used. All the compounds were non-electrolytes.

Magnetic-susceptibility Measurements.—These were done (on the finely powdered solids) with a Gouy-type balance. The effective magnetic moments, $\mu_{eff.}$, were calculated from the susceptibilities at room temperature. The susceptibility values are listed in Table 2.

Absorption Spectra.—The spectra of solutions were measured at room temperature on a Beckman Ratio Recording spectrophotometer over the range 300—1000 mμ. The complete spectrum was obtained by using about 10^{-3}M-solutions for the range 700—1000 mμ, and about 10^{-4}M-solutions for the range 300—700 mμ.

The reflection spectra of the finely powdered solids were measured on a Unicam S.P. 500 spectrophotometer fitted with a Unicam diffuse reflection attachment, S.P. 540; magnesium carbonate was the reference standard.

The values of $\lambda_{max.}$ and the corresponding extinction coefficients are listed in Table 3. The intensity of absorption in the reflection spectra is given on an arbitrary scale, *D*, which varies from compound to compound.

Measurement of Electric Dipole Moments.—These were determined as described in Part I. The molar refraction R_D was evaluated from tables, the values used (in c.c.) being: Ni = 18·8;[21] C_6H_5 = 21·5, Bu^n = 19·5; SCN = 13·6; Cl = 9·1; Br = 8·9; I = 13·9; NO_3 = 9·1;[22] P = 9·1.[23]

The experimental data are listed in Table 4. The dipole moment (μ 15%) values reported were calculated after allowance for the atom polarization: $P_A = 15\% P_E$.

TABLE 4. *Electric dipole moments.*

$(Bu^n_2PhP)_2NiCl_2$			$(Bu^n_2PhP)_2NiBr_2$			$(Bu^n_2PhP)_2NiI_2$		
10^6w_2	ε_{12}	v_{12}	10^6w_2	ε_{12}	v_{12}	10^6w_2	ε_{12}	v_{12}
—	2·2750	1·14468	—	2·2750	1·14470	—	2·2750	1·14473
2075	2·2764	1·1443	893	2·2757	1·14446	1208	2·2773	1·14411
3702	2·2774	1·14409	1387	2·2762	1·14421	1474	2·2777	1·14404
4181	2·2778	1·14391	2129	2·2771	1·14404	2242	2·2791	1·14373
			2814	2·2778	1·14366	2797	2·2802	1·14342
$\varepsilon_{12} = 2·2750_2 + 0·660w_2$			$\varepsilon_{12} = 2·2748_9 + 1·017w_2$			$\varepsilon_{12} = 2·2750_1 + 1·845w_2$		
$v_{12} = 1·1446 - 0·173w_2$			$v_{12} = 1·1447 - 0·362w_2$			$v_{12} = 1·1447_1 - 0·457w_2$		
${}_TP_2$ = 238 c.c.			${}_TP_2$ = 281 c.c.			${}_TP_2$ = 418 c.c.		
${}_EP_2$ = 177 c.c.			${}_EP_2$ = 183 c.c.			${}_EP_2$ = 193 c.c.		
μ 15% = 1·3 ± 0·1D			μ 15% = 1·9 ± 0·15D			μ 15% = 3·1 ± 0·1D		

[21] Bentley and Sutton, *Nature*, 1932, **130**, 314.
[22] Landolt–Börnstein, "Tabellen," 1951.
[23] Jones, Davies, and Dyke, *J. Phys. Chem.*, 1933, **37**, 853.

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TABLE 4. (*Continued.*)

$(Bu^n_2PhP)_2Ni(NO_3)_2$

10^6w_2	ε_{12}	ν_{12}
—	2·2750	1·14468
873	2·2893	1·14440
2405	2·3158	1·14398
2932	2·3246	1·14391
3758	2·3387	1·14367

$\varepsilon_{12} = 2{\cdot}2747_9 + 17{\cdot}00w_2$
$\nu_{12} = 1{\cdot}14465 - 0{\cdot}264w_2$
$_TP_2$ = 2169 c.c.
$_MP_2$ = 183 c.c.
μ 15% = 9·8 ± 0·1D

$(Bu^n_2PhP)_2Ni(SCN)_2$

10^6w_2	ε_{12}	ν_{12}
—	2·2750	1·14468
1666	2·2766	1·14433
1834	2·2768	1·14430
2504	2·2773	1·14416
2951	2·2779	1·14398

$\varepsilon_{12} = 2{\cdot}2750_0 + 0{\cdot}961w_2$
$\nu_{12} = 1{\cdot}1447_0 - 0{\cdot}227w_2$
$_TP_2$ = 281 c.c.
$_EP_2$ = 192 c.c.
μ 15% = 1·8 ± 0·1D

$(Bu^n_2Ph_2P)_2NiCl_2$

10^6w_2	ε_{12}	ν_{12}
—	2·2750	1·14467
2432	2·2814	1·14363
2776	2·2821	1·14359
4077	2·2857	1·14318
5402	2·2891	1·14242

$\varepsilon_{12} = 2{\cdot}2749_8 + 2{\cdot}614w_2$
$\nu_{12} = 1{\cdot}1446_2 - 0{\cdot}402w_2$
$_TP_2$ = 438 c.c.
$_EP_2$ = 188 c.c.
μ 15% = 3·3 ± 0·1D

$(Bu^n_2Ph_2P)_2NiBr_2$

10^6w_2	ε_{12}	ν_{12}
—	2·2750	1·14468
1189	2·2822	1·14419
3065	2·2932	1·14371
4606	2·3020	1·14308
6553	2·3138	1·14218

$\varepsilon_{12} = 2{\cdot}2750_7 + 5{\cdot}895w_2$
$\nu_{12} = 1{\cdot}1447_1 - 0{\cdot}370w_2$
$_TP_2$ = 941 c.c.
$_EP_2$ = 194 c.c.
μ 15% = 5·9 ± 0·02D

$(Bu^n_2Ph_2P)_2NiI_2$

10^6w_2	ε_{12}	ν_{12}
—	2·2750	1·14468
2523	2·2920	1·14350
3805	2·3010	1·14291
4691	2·3072	1·14253
5748	2·3142	1·14218

$\varepsilon_{12} = 2{\cdot}2749_3 + 6{\cdot}844w_2$
$\nu_{12} = 1{\cdot}1446_4 - 0{\cdot}441_6w_2$
$_TP_2$ = 1192 c.c.
$_EP_2$ = 194 c.c.
μ 15% = 6·8 ± 0·02D

$(Bu^n_2Ph_2P)_2Ni(NO_3)_2$

10^6w_2	ε_{12}	ν_{12}
—	2·2750	1·14468
384	2·2812	1·14464
419	2·2817	1·14464
463	2·2824	1·14457
484	2·2827	1·14460

$\varepsilon_{12} = 2{\cdot}2749_7 + 16{\cdot}10w_2$
$\nu_{12} = 1{\cdot}1446_9 - 0{\cdot}171w_2$
$_TP_2$ = 2212 c.c.
$_EP_2$ = 195 c.c.
μ 15% = 9·8 ± 0·1D

$(Bu^n_2Ph_2P)_2Ni(SCN)_2$

10^6w_2	ε_{12}	ν_{12}
—	2·2750	1·14468
1419	2·2767	1·14429
1828	2·2771	1·14412
2112	2·2776	1·14402
2465	2·2781	1·14384

$\varepsilon_{12} = 2{\cdot}2749_6 + 1{\cdot}238w_2$
$\nu_{12} = 1{\cdot}1447_1 - 0{\cdot}330w_2$
$_TP_2$ = 313 c.c.
$_EP_2$ = 204 c.c.
μ 15% = 2·0 ± 0·1D

$\{(Cl{\cdot}CH_2)_3P\}_2NiBr_2$

10^6w_2	ε_{12}	ν_{12}
—	2·2750	1·14468
1198	2·2764	1·14388
1346	2·2765	1·14381
1519	2·2766	1·14357
2065	2·2771	1·14332

$\varepsilon_{12} = 2{\cdot}2750_6 + 1{\cdot}029w_2$
$\nu_{12} = 1{\cdot}1446_8 - 0{\cdot}672w_2$
$_TP_2$ = 193 c.c.
$_EP_2$ = 118 c.c.
μ 15% = 1·5 ± 0·2D

The authors thank Dr. J. Chatt for a gift of triethylphosphine, and Messrs. Albright and Wilson for gifts of dichlorophenylphosphine, chlorodiphenylphosphine, tetrakishydroxymethylphosphonium chloride and tetrakischloromethylphosphonium chloride. They also thank Dr. R. J. P. Williams for discussion and for the use of a magnetic susceptibility balance and a Beckman spectrophotometer, Miss M. I. Christie for the use of a Unicam spectrophotometer, and Mr. D. J. Morgan for calculating the values of μ 15%.

INORGANIC AND PHYSICAL CHEMISTRY LABORATORIES, UNIVERSITY OF OXFORD,
SOUTH PARKS ROAD, OXFORD. [*Received, December 15th*, 1960.]

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532. *The Chemistry of Extractives from Hardwoods. Part XXXII.* Adifoline, an Alkaloid from* Adina cordifolia.

By A. D. Cross, F. E. King, and T. J. King.

A new alkaloid, adifoline, $C_{22}H_{20}N_2O_8$, has been isolated from the heartwood of *Adina cordifolia*. Benzoic acid, umbelliferone, and β-sitosterol are other minor constituents. Adifoline, which contains two acidic groups, belongs to the β-carboline series and is ultimately degraded to apoadifoline, $C_8H_8N_2$, an isomer of apoharmine. Syntheses of certain indoles and oxindoles incidental to the structural problem are described.

The S.E. Asian tree *Adina cordifolia* Hook (family Rubiaceae) possesses a hard, yellow, heartwood known as keli-kadem (Bengal), haldu (N. India), or kwow (Burma and Siam). In 1938 Lal and Dutt [1] described the isolation of a yellow constituent "adinin" and attributed to it the formula $C_{16}H_{14}O_7$. The more detailed examination described here confirms the occurrence of a compound agreeing in physical properties with "adinin" which, however, is shown to be an alkaloid, $C_{22}H_{20}N_2O_8$, of the β-carboline series. In view of possible confusion with the purine adenine we have re-named the compound *adifoline*. One other *Adina* species, *A. rubrostipulata* K. Schum., has previously been examined and contains mitraphylline.[2]

An oily, light-petroleum extract of the ground heartwood, when separated into acid and neutral portions, afforded benzoic acid and β-sitosterol. Ether-extraction of the residual wood then yielded umbelliferone. Adifoline was thereafter obtained from the remaining wood by extraction with boiling acetone; the yield varied (0—0·27% of the wood); it formed bright yellow crystals, slightly soluble in, *e.g.*, ethanol, to give intensely coloured solutions with a brilliant green fluorescence.

Adifoline, $C_{22}H_{20}N_2O_8$ (but normally obtained as a trihydrate), dissolves in aqueous ammonia and sodium hydrogen carbonate, indicating presence of at least one carboxyl group, and titration gave an equivalent weight of 284. Heating it with aqueous alkali liberated acetic acid, corresponding to one acetyl group. One further oxygen atom was identified as methoxyl (Zeisel), and one *C*-methyl group in addition to that present as acetyl was detected by the Kuhn–Roth method. The presence of two acidic groups was established by the formation of a (gummy) dimethyl derivative with diazomethane or methyl sulphate and potassium carbonate. Both adifoline and the dimethyl derivative are weakly basic and dissolve sparingly in mineral acid, but none of the salts, not even derivatives of organic compounds, *e.g.*, picric acid, methyl iodide, was obtained crystalline.

Adifoline was unchanged by hydrogenation over Adams catalyst in a variety of solvents. The low solubility hampered reduction by lithium aluminium hydride, and other methods using hydrochloric acid with tin, zinc, or magnesium were also unsuccessful.

Some indications of the structure were obtained when a close resemblance was observed between the ultraviolet absorption of adifoline and that of 1-ethyl-β-carboline [3] (I; R = Me) and of yobyrine [4] (I; R = *o*-tolyl). Moreover, acidification produced absorption shifts to maxima typical of the β-carbolinium cation chromophore, as exemplified by alstonine or serpentine salts (II).[5] In each case, however, although all absorption intensity values remain strictly comparable, there is a bathochromic shift of the longest-wavelength maximum of adifoline relative to that of the reference compounds (see Table).

In the infrared spectrum of adifoline (in Nujol) measured by Dr. Meakins (Oxford),

* Part XXXI, *J.*, 1961, 702.

[1] Lal and Dutt, *J. Indian Chem. Soc.*, 1938, **12**, 257.
[2] Michiels, *J. Pharm. Belg.*, 1935, **17**, 1049.
[3] Leonard and Elderfield, *J. Org. Chem.*, 1942, **7**, 556.
[4] Pruckner and Witkop, *Annalen*, 1943, **554**, 127.
[5] Schlittler and Schwarz, *Helv. Chim. Acta*, 1950, **33**, 1463.

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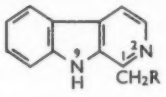
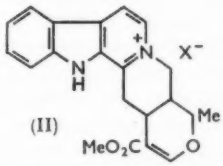
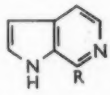
bands of medium intensity are discernible at 3510, 3330, and 3075 cm.$^{-1}$, which together with general broad absorption over the range 3570—2530 cm.$^{-1}$, suggest the presence of one or more carboxylic acid groups, while not excluding OH and NH groups.* Complex absorption occurs in the 1710—1550 cm.$^{-1}$ region with bands at 1709s, 1706s, 1689m, 1678m, 1664m, 1658m, 1638s, 1607s, and 1577 cm.$^{-1}$. Other strong bands appear at 1220



(I)



(II)



(III)

and 1124 cm.$^{-1}$, and weak or medium absorption at 1515, 1312, 1250, 1241, 1193, 1081, 1024, 812, 790, 769, and 719 cm.$^{-1}$. Complete interpretation of this multiplicity of bands is as yet impossible although the absence of absorption above 1710 cm.$^{-1}$ excludes γ-lactone, unconjugated δ-lactone or aldehyde, phenolic ester, and unconjugated ester groups from the molecular structure.

Ultraviolet spectra of adifoline and its degradation products, and of reference compounds, in ethanol unless otherwise stated.

Substance	$\lambda_{max.}$ (log ε)				Ref.
Adifoline in EtOH	235(4·59),	285(4·38),	365(3·67)		
in 0·01N-HCl–EtOH	248(4·47),	299(4·44),	418(3·79)		
in 0·01N-NaOH–EtOH	244(4·65),	269(4·56),	390(3·72)		
1-Ethyl-β-carboline (I; R = Me)	235(4·51),	286(4·20),	351(3·73)		3
Serpentine nitrate (II; X = NO_3)	252(4·5),	305(4·35),	378(3·6)		5
Apoadifoline	219(4·47),	261(3·62),	294(3·73)		
Apoharmine (III; R = Me)	220(4·49),	263(3·68),	292(3·78)		*a*
1,7-Diazaindene	—	—	288(3·92)		*b*
2-Methyl-1,4-diazaindene	—	—	297(4·0)		*b*
2-Methyl-1,5-diazaindene	—	267(3·51)	—		*b*
peri-Fused pentacyclic product (VIII) from selenium reaction	232(4·13),	266(3·89), 373(4·50),	354(4·14) 392(4·59)		
Perylene	252(4·64),	386(4·09),	407(4·43),	434(4·53)	
β-Carboline S_1 from selenium dehydrogn.	231	289	331		
Phenolic β-carboline S_2 from selenium dehydrogn.	231	297	339		
Norharman	232	285	340		4
Harmol	242	300	337		*c*
Tetrahydrocarbazole	229	282	—		*d*
Tetrahydro-6-methoxycarbazole	226	289	—		*c*
Yobyrine	237	290	237, 338, 348		4, *e*
11-Hydroxy-yobyrine	244	302	336		*f*

Refs.: *a*, Schwartz and Schlittler, *Helv. Chim. Acta*, 1951, **34**, 629. *b*, G. A. Swann, personal communication. *c*, Schlittler, Burckhardt, and Gellért, *Helv. Chim. Acta*, 1953, **36**, 1337. *d*, Beer, McGrath, and Robertson, *J.*, 1950, 2118. *e*, Schwartz, *Experientia*, 1950, **6**, 330. *f*, Dorfman, Furlemeier, Huebner, Lucas, MacPhillamy, Müller, Schlittler, and St. André, *Helv. Chim. Acta*, 1954, **37**, 59.

The absence of spectroscopic evidence for a normal *O*-acetyl group and the known instability of *N*-acetylcarbazoles and related carbolines require that the molecule of acetic acid formed on alkaline hydrolysis arises from some secondary decomposition.

Oxidation confirmed the presence of the β-carboline system disclosed by ultraviolet spectroscopy. Treatment of adifoline with alkaline permanganate yielded no identifiable products, but use of hot concentrated nitric acid led to an amorphous, weak, tetracarboxylic acid with the ferrous reaction of a pyridine-α-carboxylic acid.[6] Analysis of

* For tabulated infrared absorption frequencies and correlations with structural units, see A. D. Cross, "An Introduction to Practical Infra-red Spectroscopy," Butterworths, London, 1960.

[6] Ley, Schwartz, and Münnich, *Ber.*, 1924, **57**, 349.

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the methyl ester gave the formula $C_{16}H_{16}N_2O_8$ which contains four methoxyl (Zeisel) and one *C*-methyl group (Kuhn–Roth). Since the methoxyl content of the acid is nil, the derivative is a tetramethyl ester. It is insoluble in alkali and possesses one active hydrogen (Zerewitinoff), which is therefore present as NH. Hydrolysis with 2% aqueous sodium hydroxide regenerated the tetracarboxylic acid, but saponification with 10% alkali was accompanied by decarboxylation and resulted in a hydrated tricarboxylic acid which was readily converted into a trimethyl ester. Thermal decarboxylation of the tetracarboxylic acid gave the anhydrous tricarboxylic acid, estimations of the evolved carbon dioxide and water being consistent with $C_{12}H_8N_2O_8,2H_2O$ as the formula of the amorphous tetracarboxylic acid. The triacid was also obtained directly from adifoline by oxidation with concentrated nitric acid at 140° under pressure.

Distillation with zinc dust or freshly precipitated copper powder effected total decarboxylation of the tetracarboxylic acid, and nitrogen analysis of the resulting viscous, alkali-insoluble product, apoadifoline, was in good agreement with the expected molecular formula $C_8H_8N_2$. The ultraviolet absorption of apoadifoline very closely resembles that of apoharmine [7] (III; R = Me) (see Table) but differs noticeably from those of 1,4-, 1,5-, and 1,7-diazaindene which possess only one maximum above 250 mμ. Apoharmine and apoadifoline also exhibit similar colour changes in Dische's carbazole test.[8] The analytical and spectroscopic evidence therefore reveals 1,6-diazaindene $C_7H_6N_2$ (III; R = H) as the parent nucleus of apoadifoline and its derivatives, strong hydrogen-bonding between the NH and adjacent methoxycarbonyl groups accounting for the absence of a characteristic N–H stretching absorption band in the infrared spectrum of the tetramethyl ester.

In addition to alternatives represented by the expression (IV), structures of type (V) require consideration also for the tetracarboxylic acid since the side-chain $CH_2{\cdot}CO_2H$ would lead ultimately through decarboxylation to the generation of acetic acid in the Kuhn–Roth oxidation.

Through the co-operation of Dr. L. M. Jackman (Imperial College, London) a nuclear magnetic resonance spectroscopic study has been made of the tetramethyl ester.* A peak at 2·70 requires the presence of an aromatic hydrogen atom and thus excludes structures of type (IV) in which all available sites are substituted since the NH group is not substituted (see above). Moreover, the value 2·70 corresponds closely to that for the hydrogen at a pyridine β-position [10] (3·015) diminished by 0·2—0·3 p.p.m. owing to an α-methoxycarbonyl group.[11] α-Pyridine-hydrogen causes absorption at 1·50.[10]

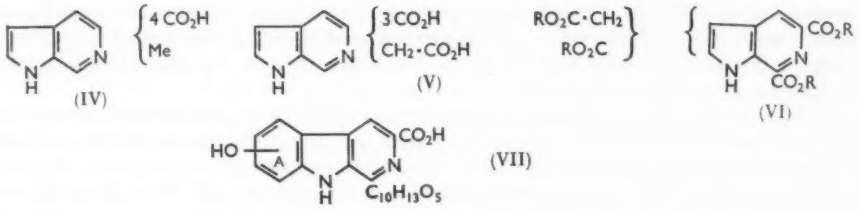
Four peaks appear in the region normally occupied by aromatic methyl ester protons, *e.g.*, 6·10 for ester-hydrogen in methyl benzoate.[12] Three of these (at 5·96, 6·03, and 6·07) are approximately equal in area, but the fourth, at 5·93, is more than half as large again. This extra absorption is attributable to the allylic methylene of $CH_2{\cdot}CO_2Me$. Shoolery's rules [13] predict that this methylene group should absorb very approximately at 6·3, but an appreciable lowering can be expected from a *cis*-α-methoxycarbonyl group [14] (compare, for example, *cis*-dimethyl β-methylglutaconate: allylic methylene absorption at 0·5 p.p.m. lower than that of the *trans*-dimethyl ester [15]). Of the various alternatives based on (IV) and (V), therefore, two isomers of structure (V) alone agree with the nuclear magnetic resonance observations. The preferred structures based on (V) appear to find

* These spectra were obtained with a solution in deuterochloroform and a Varian Associates V-4311 spectrometer with 56·4 Mc./sec. oscillator. Absorption bands are quoted as τ values.[9]

[7] Schwarz and Schlittler, *Helv. Chim. Acta*, 1951, **34**, 629; Perkin and Robinson, *J.*, 1919, **115**, 933.
[8] Dische, *Biochem. Z.*, 1927, **189**, 77.
[9] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, London, 1959, p. 47.
[10] Ref. 9, p. 64.
[11] Ref. 9, p. 123.
[12] Ref. 9, p. 55.
[13] Ref. 9, p. 59.
[14] Ref. 9, p. 121.
[15] Jackman and Wiley, *Proc. Chem. Soc.*, 1958, 196.

confirmation in the infrared absorption of the tetramethyl ester in chloroform, since of the four ester carbonyl bands (at 1713, 1718, 1722, and 1738 cm.$^{-1}$) that occurring at the significantly highest frequency may be regarded as indicating the non-conjugated carbonyl group.

Since the carboxymethylene group clearly results from the destruction of an aromatic ring, there remain only two possible structures for apoadifolinetetracarboxylic acid, namely,



those represented by formula (VI; R = H). A tentative partial structure (VII) may therefore be derived for the parent alkaloid. The expression (VII) is in agreement with conclusions based on biogenetic considerations which presume the synthesis of the carboline alkaloids from tryptophan or a related precursor. The 5-carboxyl group in (VI; R = H) corresponds to that of the tryptophan precursor, while the 7-carboxyl group is derived from the substituent—$C_{10}H_{13}O_5$ in the case of adifoline—common to all known β-carboline alkaloids. Moreover, formation of adifoline from tryptophan would leave $C_{(6)}$ of the carboline nucleus unsubstituted, in agreement with the nuclear magnetic resonance measurements on tetramethyl apodifolinetetracarboxylate.

The destruction of ring A by oxidation appears to require the presence therein of oxygenated substituents, and chemical evidence on this point was sought from selenium treatment of adifoline. This gave two oily products (S1 and S2), with the characteristic spectra of β-carbolines (see Table). S1 was non-phenolic, but product S2, though insoluble in aqueous sodium hydrogen carbonate, dissolved in sodium hydroxide solution and with ferric chloride developed a bright yellow colour. Further, the longer-wavelength ultraviolet absorption maximum of compound S2 exhibited a bathochromic shift compared with that for S1 of *ca.* 10 mμ, which is comparable with the differences observed (see Table) in the ultraviolet spectra of norharman and harmol, tetrahydrocarbazole, tetrahydro-6-methoxycarbazole, yobyrine, and 11-hydroxy-yobyrine. Compounds S1 and S2 appear to contain respectively a β-carboline and a hydroxy-β-carboline chromophore.

In contradiction to this chemical evidence, however, the ultraviolet absorption of adifoline suggests that the alkaloid A-ring is devoid of phenolic (or phenol ether) substituents, and this anomaly has yet to be resolved. High-pressure hydrogenation in butanol with Raney nickel at 200°, conditions likely to result in *N*-alkylation, afforded a product shown by ultraviolet examination of distillation and chromatographic fractions to be a mixture of indoles and indolenines. However, each fraction was insoluble in alkali, including one fraction $C_{15}H_{21}NO$ which was methoxyl-free, and had the spectrum of a typical αβ-disubstituted indole [231 (log ε 4·03), 289 mμ (log ε 3·62)].

Alkali-fusion has not yielded any recognisable product except the acetic acid obtained by milder saponification. Evidence from ultraviolet absorption data suggests that adifoline resembles the simple carbolines, *e.g.*, harmine and norharmine, in its absorption maxima and in the characteristic band shifts in acid media. The N(*b*) atom thus appears to be tertiary and part of an aromatic system and in this respect adifoline is exceptional among the more complex carboline alkaloids. Yet it is noteworthy that other evidence from light absorption, particularly in the infrared region, is compatible with the presence of a conjugated vinyl ether fragment $MeO_2C{-}C{=}C{-}O{-}$ found in several indole

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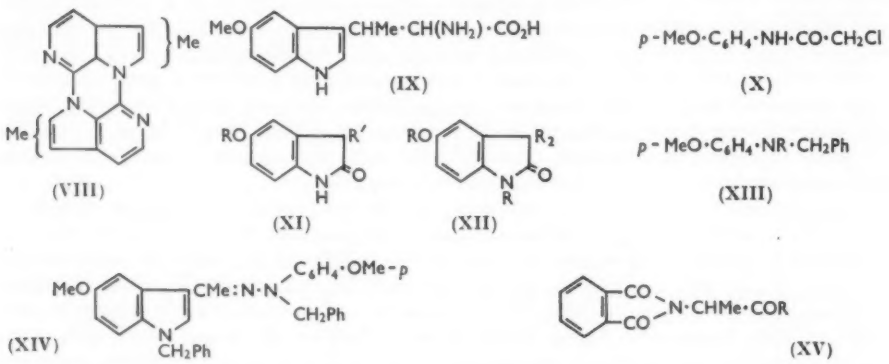
alkaloids [16] that contain a fourth ring fused to ring C *via* the nitrogen atom. Before the partial structure (VII) can be extended, further experimental work is required. This unfortunately has been precluded by difficulties in finding wood samples containing significant amounts of the alkaloid.

When apoadifolinetetracarboxylic acid was heated with selenium a small quantity of a product was isolated having an ultraviolet absorption of general resemblance to that of perylene (see Table). This result may be interpreted as the "*peri*"-fusion of two 1,6-diazaindene residues at the 1- and 7-positions to yield the hitherto unknown heterocycle, 5,5*b*,10,10*b*-tetrazadicyclopent[*de*,*kl*]anthracene,* carrying two methyl substituents (VIII), and it affords further support for the conclusion that the 7-position of apoadifoline cannot bear a *C*-methyl substituent.

Indole and Oxindole Syntheses.—Before nuclear magnetic resonance spectrometry had eliminated a methoxy-α-methyltryptophan structure, *e.g.*, (IX), as a possible adifoline precursor three synthetic routes to this amino-acid were explored. In the first, *N*-chloroacetyl-*p*-anisidine [17] (X) was converted into 5-hydroxyoxindole (XI; R = R′ = H) by a modification of the Stollé method,[18] and 5-methoxyoxindole (XI; R = Me, R′ = H) (35%) accompanied by 5-methoxy-1,3,3-trimethyloxindole (XII; R = Me) obtained from



it with dimethyl sulphate. Others [19] obtained unsatisfactory yields of 5-hydroxyoxindole with the standard Stollé procedure.[20] The properties of 5-methoxyoxindole agree with those of the product previously prepared by cyclisation of 2-amino-5-methoxyphenylacetic acid; [21] Robertson and his co-workers [19] have already shown that the compound prepared by Giovannini and Portmann [22] using vigorous conditions in the Stollé synthesis is in fact 5-hydroxyoxindole, as suggested earlier by Julian *et al.*[23]

Acetylation of 5-methoxyoxindole with sodium ethoxide and ethyl acetate [24] gave 3-acetyl-5-methoxyoxindole (XI; R = Me, R′ = Ac) but the acetyl group was removed during attempted preparation of the ethylene ketal required for conversion into the corresponding indole. With cold acetic anhydride–pyridine 5-hydroxyoxindole was converted

* Ring Index nomenclature, suggested by the Editor.

[16] Janot and Goutarel, *Bull. Soc. chim. France*, 1951, 588; Bader, *Helv. Chim. Acta*, 1953, **36**, 215.
[17] Hill and Kelsey, *J. Amer. Chem. Soc.*, 1922, **44**, 2357.
[18] Abramovitch and Hey, *J.*, 1954, 1697.
[19] Beer, Davenport, and Robertson, *J.*, 1953, 1262; Kellie, O'Sullivan, and Sadler, *J.*, 1956, 3809.
[20] Stollé, *Ber.*, 1914, **47**, 2120.
[21] Koelsch, *J. Amer. Chem. Soc.*, 1944, **66**, 2019.
[22] Giovannini and Portmann, *Helv. Chim. Acta*, 1948, **31**, 1381.
[23] Julian, Meyer, and Printy, in Elderfield's "Heterocyclic Compounds," Wiley, New York, 1952, Vol. III, p. 145.
[24] Horner, *Annalen*, 1941, **548**, 117.

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into 5-acetoxy-1,3,3-triacetyloxindole (XII; R = Ac). The preparation and light absorption of some 3-acyl-5-methoxyindoles have been reported recently.[25]

A novel approach to 3-acetyl-5-methoxyindole was investigated in which an *N*-benzyl substituent was incorporated to exclude pyrazole formation during a Fischer indole reaction of the appropriate hydrazone (XIII; R = N:CH·CH_2·COMe). *N*-Benzyl-*p*-anisidine was prepared from *N*-benzylidene-*p*-anisidine by three reduction methods (see Experimental section). Low hydrogenation temperatures were necessary since those recommended for hydrogenation of azomethines [26] caused debenzylation. The amine (XIII; R = H) was converted into *N*-benzyl-*N*-nitroso-*p*-anisidine (XIII; R = NO), and the nitrosamine reduced with lithium aluminium hydride [27] to *N*-benzyl-*N*-*p*-methoxyphenylhydrazine (XIII; R = NH_2), which was characterised as its hydrochloride and benzylidene and *p*-nitrobenzylidene derivatives. Other reduction procedures gave low yields, or cleaved the N–N bond, forming the amine (XIII; R = H). The weakness of the N–N bond was illustrated in the reaction of the hydrazine (XIII; R = NH_2) with the sodio-derivative of acetylacetaldehyde [28] in cold aqueous acetic acid, in which Fischer indole cyclisation rapidly occurred. Formation of 3-acetyl-1-benzyl-5-methoxyindole as its *N'*-benzyl-*N'*-*p*-methoxyphenylhydrazone (XIV) under these extremely mild reaction conditions is unusual. Other products isolated from the reaction mixture were *N*-benzyl-*p*-anisidine (XIII; R = H) and benzaldehyde *N'*-benzyl-*N'*-*p*-methoxyphenylhydrazone (XIII; R = N:CHPh); these two products apparently come from a disproportionation of either the hydrazine (XIII; R = NH_2) or the initial hydrazone (XIII; R = ·N:CH·CH_2·COMe) to give *N*-benzyl-*p*-anisidine and *N*-benzylidene-*p*-anisidine, cleavage of the latter yielding *p*-anisidine (not isolated) and benzaldehyde as the source of (XIII; R = ·N:CHPh). This synthetic route was therefore abandoned.

α-Phthalimidopropionic acid (XV; R = OH), prepared from phthalic anhydride and DL-alanine, was converted by thionyl chloride quantitatively into α-phthalimidopropionyl chloride [29] (XV = Cl). This acid chloride and indolylmagnesium bromide produced 3-α-phthalimidopropionylindole (XV; R = 3-indolyl) in only 3% yield, insufficient to merit further investigation of this route to the desired tryptophan.

Syntheses have since been announced of α-methyltryptophan, involving a Mannich reaction of indole with an appropriate ketimine,[30] and of α-methyltryptamine.[31]

Experimental

Except where otherwise stated, ultraviolet absorption spectra were measured for ethanol solutions with a Unicam S.P. 500 spectrophotometer, and analytical samples of solids were dried at 120° in a vacuum for 3 hr. Rotations are for chloroform solutions. Light petroleum refers to the fraction of b. p. 60—80°. Figures for light absorption are $\lambda_{max.}$ in mμ followed by log ε in parentheses.

Extraction of Adina cordifolia *Heartwood.*—Continuous extraction of the coarsely powdered heartwood (12 kg.) with boiling light petroleum for 24 hr. afforded a yellow-brown syrup (11 g., 0·09%). Benzoic acid was obtained from an ether solution of the syrup by extraction with sodium hydrogen carbonate. The recrystallised acid (1·68 g.), its anilide, and its *p*-bromophenacyl ester had m. p.s in accord with those of authentic preparations and gave no depression on admixture therewith.

After extraction with aqueous 2N-alkali and with 2N-acid the dried ether solution was evaporated to yield a neutral oil from which, by chromatography on alumina, " β "-sitosterol was separated as plates (from methanol), m. p. 136—137°, $[\alpha]_D$ −34° (*c* 0·47). In the

[25] Ballantine, Barrett, Beer, Boggiano, Eardley, Jennings, and Robertson, *J.*, 1957, 2227.
[26] Magee and Henze, *J. Amer. Chem. Soc.*, 1940, **62**, 910.
[27] Schueler and Hanna, *J. Amer. Chem. Soc.*, 1952, **74**, 3693.
[28] Johnson, Woroch, and Mathews, *J. Amer. Chem. Soc.*, 1947, **66**, 566.
[29] Gabriel, *Ber.*, 1905, **38**, 630.
[30] Snyder and Matteson, *J. Amer. Chem. Soc.*, 1957, **79**, 2217.
[31] Abramovitch and Muchowski, *Canad. J. Res.*, 1960, **38**, 554.

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Liebermann–Burchard test this sterol underwent the colour changes, red ⟶ purple ⟶ blue ⟶ green. The derived acetate [32] had m. p. 127·5—128·5° [Found: C, 81·3; H, 11·4%; *M* (Rast), 455. Calc. for $C_{31}H_{52}O_2$: C, 81·6; H, 11·4%; *M*, 456·5], and the benzoate [32] had m. p. 144—145° (Found: C, 83·1; H, 10·2. Calc. for $C_{36}H_{54}O_2$: C, 83·3; H, 10·5%).

The wood was next extracted with boiling ether for 24 hr. A gum containing crystals was obtained. Crystallisation from hot water (charcoal) afforded prisms of umbelliferone (7-hydroxycoumarin), m. p. 227—228° (0·03% of the wood) [Found: C, 66·5; H, 4·1%; *M* (Rast), 168. Calc. for $C_9H_6O_3$: C, 66·7; H, 3·7%; *M*, 162]. The coumarin gave an acetate, m. p. 140°, and a methyl ether (treatment with diazomethane), m. p. 116° (Found: C, 67·9; H, 4·9; OMe, 16·7. Calc for $C_{10}H_8O_3$: C, 68·2; H, 4·6; 1OMe, 17·6%), and with aqueous bromine a tribromo-derivative, pale yellow rods (from ethanol), m. p. 197—198° (Found: C, 26·9; H, 1·0; Br, 59·5. Calc. for $C_9H_3Br_3O_3$: C, 27·1; H, 0·8; Br, 60·1%). These physical constants are in close agreement with those recorded [33] for umbelliferone and its derivatives.

Finally, the ground wood was extracted with boiling acetone during 24 hr., and the extract treated in one of two ways. Either it was evaporated, and the residual gum (90—120 g. per 3 kg. of wood) leached with warm water (2 l.) and dissolved in glacial acetic acid (30 c.c.), whereupon crude yellow solid (0—5·1 g.) separated slowly from the syrupy solution ; or the extracts were concentrated to 300—400 c.c. and set aside; after 2—3 days crude alkaloid separated, and further quantities of alkaloid were collected at intervals until no further separation occurred on further concentration. In later extractions, ground heartwood was extracted directly with hot acetone, the light petroleum and ether extractions being omitted, and the yellow principle was obtained from the concentrated extracts as outlined above.

Adifoline.—Crude alkaloid from the modified extraction procedure was extracted successively in a Soxhlet apparatus with benzene (3 days) and ether (3 days). Recrystallisation of the residue several times from ethanol or acetic acid afforded pure *adifoline* as small bright yellow needles or prisms, respectively, which did not melt but darkened slowly above 183° and blackened rapidly at 195—196° with shrinking (Found: C, 53·6; H, 5·6; N, 5·7; OMe, 6·3; Ac, 8·3; *C*-Me, 4·9%; equiv., 284. $C_{22}H_{20}N_2O_8,3H_2O$ requires C, 53·4; H, 5·3; N, 5·7; 1OMe, 6·3; 1Ac, 8·7; 2*C*-Me, 6·1%; equiv., 247). The water of crystallisation was removed at 150° *in vacuo* (Found: C, 60·1; H, 5·1; N, 6·6; OMe, 6·25. $C_{22}H_{20}N_2O_8$ requires C, 60·0; H, 4·8; N, 6·4; OMe, 7·0%). Both sets of analyses agree less well for a formula $C_{22}H_{22}O_8N_2$ for adifoline. Accurate determination of the equivalent weight by titration was hindered by the intense yellow colour of solutions of the alkaloid, which masked the end-point (phenolphthalein).

Neither a picrate nor a methiodide of adifoline could be prepared, nor could crystalline salts be obtained with oxalic, perchloric, sulphuric, nitric, hydrochloric, or hydriodic acid, or with brucine, strychnine, cinchonine, piperidine, triethylamine, or morpholine. Adifoline gave no carbonyl derivatives; negative reactions with ferric chloride, in tests for methylenedioxy, and in the Ehrlich test for indoles were obtained.

Methylation of Adifoline.—(a) *With diazomethane.* An ice-cold solution of adifoline (0·5 g.) in butan-1-ol (175 c.c.) was treated repeatedly with an excess of ethereal diazomethane. After removal of the ether, the alcoholic solution was boiled (charcoal) and evaporated. The residual gum gave a yellow solution in ethanol with an intense green fluorescence. A solution of the product in benzene (100 c.c.) was washed with aqueous 2N-alkali and with water, dried, and concentrated to 40 c.c. before being placed on a column of alumina (20 g.). Elution with benzene–ether (2 : 1) afforded *adifoline dimethyl ester* as a clear, yellow, alkali-insoluble glass (0·31 g., 65%) (Found, for a specimen purified by further chromatography: OMe, 17·9. $C_{24}H_{24}N_2O_8$ requires 3OMe, 19·9%), $\lambda_{max.}$ 240 (4·48), 282 (4·48), 352 mμ (3·69). The ester had the same solubilities in dilute or concentrated mineral acid as had adifoline itself.

(b) *With dimethyl sulphate.* Adifoline was methylated in boiling acetone solution with dimethyl sulphate–potassium carbonate, and the viscous oily product thus obtained chromatographed as described above. Adifoline dimethyl ester, after rechromatography, was gained as a clear yellow glass (Found: OMe, 18·5%).

Oxidation of Adifoline.—A solution of adifoline (1·17 g.) in nitric acid (75 c.c.; *d* 1·4) was heated on the steam-bath for 20 hr. and then evaporated under reduced pressure. More nitric

[32] King and Jurd, *J.*, 1953, 1192.
[33] Markley, Nelson, and Sherman, *J. Biol. Chem.*, 1937, **118**, 433.

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acid (75 c.c.; *d* 1·4) was added and the procedure repeated. Water (50 c.c.) was then added to the residues and the mixture boiled for 0·5 hr. before it was again evaporated to dryness under reduced pressure. A solution of the pale yellow residue (0·53 g.) in boiling water was filtered and allowed to cool; over a period of several days, three or four crops of nearly colourless, amorphous apoadifolinetetracarboxylic acid (0·468 g.) were collected (Found: OMe, absent). The acid, which effervesced at 223—225° without melting, dissolved readily in dilute aqueous sodium hydrogen carbonate and sparingly in dilute mineral acid, but was practically insoluble in the usual organic solvents. It gave a negative test with ferric chloride, but an aqueous solution with ferrous sulphate produced a red-brown colour.[6]

Methylation of the Tetracarboxylic Acid.—(*a*) Diazomethane and the tetracarboxylic acid in methanolic suspension gave *tetramethyl apoadifolinetetracarboxylate* as needles (from ethanol), m. p. 210—211° [Found: C, 52·9; H, 4·1; N, 7·6; OMe, 34·1; *C*-Me, 3·7; active H, 0·28%; *M* (Rast), 368. $C_{16}H_{16}N_2O_8$ requires C, 52·8; H, 4·4; N, 7·7; 4OMe, 34·1; 1*C*-Me, 4·1; 1H, 0·28%; *M*, 364]. Ethanolic solutions of the ester fluoresced strongly blue. Light absorption was at 240 (4·69) and 296 mμ (3·97). The infrared spectrum showed no band between 3200 and 3570 cm.$^{-1}$.

(*b*) Dimethyl sulphate (4 c.c.), potassium carbonate (10 g.), and the tetracarboxylic acid (1 g.) were heated together in boiling acetone (150 c.c.) for 24 hr. More dimethyl sulphate (4 c.c.) was added and boiling continued a further day. The tetramethyl ester (686 mg.) was isolated from the filtered mixture by concentration and crystallisation.

Apoadifolinetricarboxylic Acid.—(*a*) The tetracarboxylic acid (250 mg.) and nitric acid (25 c.c.; *d* 1·4) were heated together at 140° in a sealed Carius tube for 20 hr. Crystals separated from the cooled solution. These were collected and the filtrate evaporated to give a residue which recrystallised from water. Further recrystallisations of the solids afforded *apoadifolinetricarboxylic acid* as a monohydrate, pale yellow prisms (64 mg.), m. p. 308—310° (Found: C, 46·6; H, 3·8; N, 10·3. $C_{11}H_8N_2O_8,H_2O$ requires C, 46·8; H, 3·6; N, 9·9%). The anhydrous *acid* was obtained as an amorphous powder, decomp. >300°, when the monohydrate was dried to constant weight at 160° (Found: C, 49·6; H, 3·2; loss in wt., 7·2. $C_{11}H_8N_2O_8$ requires C, 50·0; H, 3·05; loss in wt., 6·4%).

(*b*) Adifoline (1 g.) was heated with nitric acid (30 c.c.; *d* 1·4) in a sealed Carius tube at 140° for 24 hr. and apoadifolinetricarboxylic acid (134 mg.) isolated as described above.

Thermal Decarboxylation of Apoadifolinetetracarboxylic Acid.—Apoadifolinetetracarboxylic acid (300 mg.) was heated at 225° (oil-bath) in a slow stream of carbon dioxide-free, oxygen-free, dry nitrogen, and the effluent nitrogen bubbled through standard barium hydroxide solution. The oil-bath temperature was maintained at 225° until effervescence had diminished and then increased to 250° for 5 min. Carbon dioxide evolved was estimated by titration of the excess of baryta against standard hydrochloric acid (phenolphthalein). The amorphous residue (218 mg.) gave no colour with ferrous sulphate and, on crystallisation from water, afforded pale-yellow prisms, m. p. 312—314° undepressed on admixture with the hydrated tricarboxylic acid [Found: CO_2 evolved, 49·2 mg.; water of crystallisation lost (by difference), 32·8 mg. Calc. for $C_{12}H_8N_2O_8,2H_2O$: loss of $1CO_2$, 43 mg.; loss of $2H_2O$, 31·4 mg.].

Esterification of the Tricarboxylic Acid.—Ethereal diazomethane converted the tricarboxylic acid into the *trimethyl ester*, needles (from methanol), m. p. 196—197° (Found: OMe, 30·5. $C_{14}H_{14}N_2O_8$ requires 3OMe, 30·0%).

Saponification of the Tetramethyl Ester.—(a) *With 10% alkali.* The tetramethyl ester (0·40 g.) and 10% aqueous sodium hydroxide (10 c.c.) were heated together on the steam-bath for 2 hr. After filtration, the yellow solution was made just acid to litmus, methanol was added to the hot solution to incipient precipitation, and the solution allowed to cool. Crystallisation of the precipitated solid from aqueous methanol yielded apoadifolinetricarboxylic acid as its monohydrate, prisms (0·28 g.), m. p. 318—320° (Found: C, 47·1; H, 3·9; N, 9·9; *C*-Me, 5·55%; equiv., 87·3. Calc. for $C_{11}H_8N_2O_8,H_2O$: *C*-Me, 5·3%; equiv., 94).

(b) *With 2% alkali.* 2% Aqueous potassium hydroxide (25 c.c.) and the tetramethyl ester (190 mg.) were heated together at 100° for 0·5 hr. and an amorphous carboxylic acid (154 mg.) was isolated from the solution by neutralisation, evaporation, and leaching out of inorganic material from the residue with cold water. The acid was identified as apoadifolinetetracarboxylic acid by converting it into the tetramethyl ester, m. p. and mixed m. p. 209—210°.

Neither the tetramethyl ester nor the tricarboxylic acid gave condensation products with benzaldehyde or *p*-nitrobenzaldehyde when piperidine was used as a catalyst.

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Apoadifoline.—An intimate mixture of clean, dry, activated zinc dust (6 g.) and finely powdered apoadifolinetetracarboxylic acid (200 mg.) was placed in the bulb of a microdistillation tube and covered with a layer of the pure zinc dust. Distillation was effected at atmospheric pressure, with gradual heating to 270° (0·5 hr.). Freshly precipitated copper powder replaced zinc dust in a similar experiment. In both cases, a small quantity of *apoadifoline* distilled over as a nearly colourless, viscous oil, b. p. 222° (bath)/755 mm. on redistillation (Found: N, 21·5. $C_8H_8N_2$ requires N, 21·2%), $\lambda_{max.}$ 219 (4·47), 261 (3·62), 294 mμ (3·73).

Addition of a trace of formaldehyde to a solution of apoadifoline in concentrated sulphuric acid (Dische's carbazole test) gave a yellow-brown colour accompanied by a green fluorescence. When diluted, the solution became colourless and fluoresced pale violet. Apoharmine shows the same colour changes.[34]

Action of Selenium on the Tetracarboxylic Acid.—Apoadifolinetetracarboxylic acid (0·70 g.) and selenium powder (2 g.) were kept at 280—290° for 20 hr. and then extracted with ether (Soxhlet) overnight. Evaporation of the filtered extracts afforded an oil (44 mg.), which was dissolved in benzene for chromatography on alumina (3 g.). Evaporation of the benzene eluate left a small quantity of pale yellow prisms, m. p. 203—205° after two recrystallisations from benzene. The prisms, believed to be a dimethyl 5,5*b*,10,10*b*-tetra-azadicyclopent[*de*,*kl*]-anthracene (VIII), showed light absorption at 232 (4·13), 266 (3·89), 354 (4·13), 372 (4·50), 392 mμ (4·59) (log ε values for $C_{16}H_{12}N_4$).

Selenium Dehydrogenation of Adifoline.—Adifoline (2 g.) and selenium (2 g.) were heated gradually to 250° and after 0·25 hr. thereat were heated at 300—310° for 0·75 hr. The cooled tube and its contents were crushed, mixed with sand, and extracted (Soxhlet) successively with benzene, ether, and methanol, each extraction being for 24 hr. Evaporation of the benzene extracts afforded a neutral yellow oil (16 mg.), purified by elution with benzene from an alumina column, but showing a negative reaction in the Ehrlich test for indoles. Negligible material resulted from ether-extraction. A yellow-brown gum (123 mg.) was obtained by evaporation of the methanol extracts. After passage through alumina this gum (75 mg.) was fractionally distilled under reduced pressure. The lower-boiling fraction constituted a viscous, colourless oil (10 mg.), b. p. 182—184° (bath)/0·01 mm., insoluble in alkali but dissolving in dilute mineral acids. An ethanolic solution showed no change in light absorption pattern on addition of alkali, and no colour developed on addition of ferric chloride. The higher-boiling fraction was a clear, yellow gum (25 mg.), b. p. 225—235° (bath)/0·03 mm., which was readily soluble in dilute aqueous sodium hydroxide but insoluble in carbonate or sodium hydrogen carbonate solution. Ethanolic solutions, light yellow in colour with intense green-blue fluorescence, became deep yellow on addition of ferric chloride. Insufficient was available for further investigations (Found: OMe, absent). Neither fraction crystallised. Light absorption data are given in the Discussion section.

Hydrogenation of Adifoline.—Anhydrous adifoline (1·2 g.) in dry butan-1-ol (240 c.c.) was hydrogenated at 200°/200 atm. over Raney nickel (*ca.* 1 g.) during 10 hr. Evaporation of the filtered solution yielded oils (1·05 g.) which were promptly chromatographed on alumina (30 g.). Acetone removed a yellow oil (*A*, 536 mg.), acetone–ethanol (1 : 1) eluted a yellow-brown oil (B, 384 mg.), and ethanol eluted a brown gum (C, 97 mg.). No single substance could be isolated from the second (B; $\lambda_{max.}$ 213, 245, 251, 285) or third (C) components from the column.

The yellow oil (A) was separated by vacuum-distillation into a mobile, yellow oil, b. p. 105—110° (bath)/0·01 mm. [Found: OMe, absent; *M* (Rast), 190], and a viscous, yellow oil, b. p. 143—148° (bath)/0·01 mm. [Found, for a sample purified by further distillation: C, 77·8; H, 9·4; N, 6·0%, OMe, absent; *M* (Rast), 211. $C_{15}H_{21}NO$ requires C, 77·9; H, 9·1; N, 6·1%; *M*, 231]. Formulation of the lower-boiling oil as a 2,3-disubstituted *N*-butylindoline was compatible with the ultraviolet spectrum ($\lambda_{max.}$ 208, 253, 280). The higher-boiling fraction had a typical αβ-disubstituted indole spectrum (see Discussion section).

None of the hydrogenation products dissolved in alkali, and none gave a positive reaction with ferric chloride.

Similar results were obtained when the hydrogenation was performed on a solution in dioxan with the expected exception that no *N*-alkylated products appeared.

Action of Alkali on Adifoline.—Adifoline (430 mg.) was boiled in aqueous 2N-sodium

[34] Lawson, Perkin, and Robinson, *J.*, 1924, **125**, 646.

hydroxide (25 c.c.) for 1 hr. The mixture was acidified, and distilled, water being added at the same rate as distillate was collected. The organic acid in the distillate (500 c.c.) was neutralised by titration against 0·02N-sodium hydroxide, and the sodium salt (50 mg.), which remained on evaporation, was boiled with ethanolic *p*-bromophenacyl bromide (15 mg. in 2 c.c.). A crystalline ester was collected which, after recrystallisation from ethanol, had m. p. 85°, alone or on admixture with *p*-bromophenacyl acetate. The acid reaction solution, after removal of the acetic acid in the aqueous distillate, was neutralised. Orange-brown solids which were precipitated were filtered off and extracted with a large volume of ethanol (charcoal). Evaporation of the extracts afforded a solid, purified by reprecipitation from aqueous ethanol to give a yellow amorphous solid which darkened at 258—261° (Found, for a specimen dried at 150°: OMe, absent; equiv., 242).

Some Unsuccessful Experiments.—No crystalline product was obtained when adifoline was treated at 100° with acetic anhydride and pyridine, sulphuric acid, perchloric acid, or acetic acid–sodium acetate.

No hydrogenation products of adifoline proved isolable when Adams platinum catalyst was used in ethanol or acetic acid at room or elevated temperatures. Chemical methods attempted included zinc, magnesium, and tin with acid; sodium and liquid ammonia; and lithium aluminium hydride in tetrahydrofuran (Soxhlet extractor technique). Adifoline dimethyl ester was unchanged after 24 hr. with the last reagent in ether.

5-Hydroxyoxindole.—*N*-Chloroacetyl-*p*-anisidine (25·0 g.) was added to a vigorously stirred melt of aluminium chloride (100 g.) and sodium chloride (20 g.) at 140°. Rapid heating to 235—240° caused brisk evolution of hydrogen chloride, but this slackened after 3—5 min. Care was taken to prevent a temperature rise to above 245° since this caused decomposition of the oxindole. The hot melt was poured on to a marble slab, allowed to cool, pulverised, and decomposed by addition to crushed ice containing a little dilute hydrochloric acid. A yellow solid was collected, washed with small quantities of water and a minimum of cold ethanol, and recrystallised from ethyl acetate (charcoal) as nearly colourless prisms of 5-hydroxyoxindole (8·44 g., 45%), m. p. 270° (decomp.) on rapid heating. The compound decomposed without melting at 252—254° when heated slowly (Found: C, 64·4; H, 4·5; N, 9·1. Calc. for $C_8H_7NO_2$: C, 64·4; H, 4·7; N, 9·4%).

Methylation of 5-Hydroxyoxindole.—5-Hydroxyoxindole (5·1 g.), when boiled with dimethyl sulphate (4·3 g.) and potassium carbonate (12 g.) in acetone during 24 hr., gave, on filtration and evaporation, an oil which crystallised from benzene (charcoal) as pale pink rods of 5-methoxyoxindole (1·93 g., 35%), m. p. 149—151° (Found: C, 66·2; H, 5·3. Calc. for $C_9H_9NO_2$: C, 66·3; H, 5·2%). Koelsch [21] recorded m. p. 152—154°.

When an excess (1·1—1·3 mol.) of dimethyl sulphate had been employed in the same procedure the oily product was fractionally distilled. The second fraction, b. p. 178—198° (bath)/0·8 mm., when triturated with ethanol, afforded *5-methoxy-1,3,3-trimethyloxindole* (1·85 g.), yellow plates (from benzene–light petroleum), m. p. 191—193° (Found: N, 7·2; OMe, 15·4. $C_{12}H_{15}NO_2$ requires N, 6·8; 1OMe, 15·1%). The oil remaining in the mother-liquors and the first fraction, b. p. 149—177° (bath)/0·08 mm., crystallised from benzene to give 5-methoxyoxindole (1·28 g.).

3-Acetyl-5-methoxyoxindole.—Ethyl acetate (0·43 g.) and 5-methoxyoxindole (0·40 g.) were added to sodium (0·06 g.) in dry ethanol (1·5 c.c.) and heated at 100° until a thick paste developed (12—15 min.). The mixture was broken up immediately with crushed ice (20 g.) containing 2N-hydrochloric acid (5 c.c.), and the precipitate collected and washed with a little water. The *3-acetyl-5-methoxyoxindole* (0·23 g.) thus obtained crystallised from aqueous ethanol as pale yellow needles, which gave a purple colour with ferric chloride and had m. p. 181° (Found: C, 64·1; H, 5·6; N, 7·3. $C_{11}H_{11}NO_3$ requires C, 64·4; H, 5·4; N, 6·8%). The *2,4-dinitrophenylhydrazone* separated from benzene–acetone as orange prisms, m. p. 256—257° (decomp.) (Found: C, 53·4; H, 3·8. $C_{17}H_{15}N_5O_6$ requires C, 53·0; H, 3·9%).

5-Methoxyoxindole was isolated from attempted ethylene ketal formation of 3-acetyl-5-methoxyoxindole. The latter (0·74 g.) was treated with boiling benzene (50 c.c.), ethylene glycol (3 c.c.), and toluene-*p*-sulphonic acid (0·15 g.) for 5 hr., and the cooled mixture treated with saturated sodium hydrogen carbonate solution. 5-Methoxyoxindole (0·42 g.) was obtained from the benzene layer.

Acylation of 5-Hydroxyoxindole.—Acetylation of 5-hydroxyoxindole with acetic anhydride–pyridine at room temperature gave *5-acetoxy-1,3,3-triacetyloxindole*, crystallising from benzene

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in needles, m. p. 204—205° (Found: C, 60·9; H, 4·9; N, 4·57; Ac, 57·2. $C_{16}H_{15}NO_6$ requires C, 60·6; H, 4·7; N, 4·4; 4Ac, 54·3%). This compound was alkali-insoluble and gave no colour with ferric chloride.

N-*Benzyl*-p-*anisidine*.—(*a*) A hot, stirred, ethanolic solution of *N*-benzylidene-*p*-anisidine was treated portionwise with sodium and, after one hour's boiling, ethanol was removed and water added. The yellow oil obtained by extraction with ether had b. p. 160—164°/0·6 mm. and crystallised from light petroleum as plates of *N*-benzyl-*p*-anisidine, m. p. 52° (yield 88%).

(*b*) *N*-Benzylidene-*p*-anisidine was reduced in ethereal solution with lithium aluminium hydride, and the mixture worked up in the normal manner. *N*-Benzyl-*p*-anisidine was isolated by extraction with ether and crystallised from ethanol as plates, m. p. 51—52° (86% yield).

(*c*) *N*-Benzylidene-*p*-anisidine in ethanol was shaken at 20° for 0·5 hr. with Raney nickel catalyst and hydrogen at 100 atm. *N*-Benzyl-*p*-anisidine was obtained in 93% yield. Similar experiments conducted at 60° (0·5 hr.) and 75° (0·5 hr.) afforded 37 and 0% respectively of the secondary amine. Distillation of the latter reaction solution gave a quantitative yield of *p*-anisidine, needles (from light petroleum), m. p. and mixed m. p. 56°. Ammonia gas was also formed (strong odour).

N-*Benzyl*-N-*nitroso*-p-*anisidine*.—A stirred ethanolic solution of *N*-benzyl-*p*-anisidine and sulphuric acid at 0° was treated portionwise with sodium nitrite (1 equiv.) and diluted with water. N-*Benzyl*-N-*nitroso*-p-*anisidine* was collected. This nitrosamine, needles from ethanol (charcoal), had m. p. 78° (90% yield) and gave a positive Liebermann reaction (Found: C, 69·1; H, 5·8; N, 11·3. $C_{14}H_{14}N_2O_3$ requires C, 69·4; H, 5·8; N, 11·6%).

N-*Benzyl*-N-p-*methoxyphenylhydrazine*.—(*a*) The above nitrosamine was added in ether to a boiling stirred suspension of lithium aluminium hydride in the same solvent. After being boiled for 2 hr. the mixture was worked up in the usual way, saturated sodium potassium tartrate solution being used to dissolve the inorganic precipitate. *N*-Benzyl-*N*-*p*-methoxyphenylhydrazine was obtained as a pale yellow oil (93% yield), b. p. 155—156°/0·2 mm., which decomposed slowly in air. The *hydrazine hydrochloride* separated from ethyl acetate–ethanol as needles, m. p. 146—147° (Found: C, 63·8; H, 6·5; N, 10·4; Cl, 13·4. $C_{14}H_{16}N_2O$,HCl requires C, 63·5; H, 6·8; N, 10·6; Cl, 13·4%). The *benzaldehyde hydrazone* was obtained as pale yellow needles, m. p. 119°, from an ethanolic solution of the hydrazine hydrochloride and benzaldehyde (Found: C, 79·9; H, 6·2; N, 8·8. $C_{21}H_{20}N_2O$ requires C, 79·7; H, 6·4; N, 8·9%). Similarly prepared, the p-*nitrobenzaldehyde hydrazone* crystallised from aqueous ethanol as orange needles, m. p. 134—136° (Found: C, 69·8; H, 5·0; N, 11·5. $C_{21}H_{19}N_3O_3$ requires C, 69·8; H, 5·3; N, 11·6%).

(*b*) Reduction of the nitrosamine with sodium in boiling ethanol for 0·5 hr., evaporation and extraction with ether, gave an oil which crystallised from ethanol as plates (91% yield), m. p. 51—52° alone or mixed with *N*-benzyl-*p*-anisidine. When the mother-liquors were warmed with benzaldehyde and 2N-sulphuric acid, and cooled, the above benzaldehyde hydrazone, m. p. 118°, was obtained in a quantity equivalent to 7% of hydrazine formation.

(*c*) Attempted reduction of the nitrosamine with zinc and acetic acid, with hydrogen sulphide, or catalytically failed. The starting materal was recovered or *N*-benzyl-*p*-anisidine and ammonia were formed.

Reaction of Acetylacetaldehyde with N-*Benzyl*-N-p-*methoxyphenylhydrazine*.—The sodium derivative of acetylacetaldehyde [29] (9·47 g., 0·085 mole) in ice-water (20 c.c.) was added dropwise to a cooled, stirred solution of the hydrazine (20·0 g., 0·086 mole) in acetic acid (11·0 g., 0·18 mole). The mixture was then stirred a further hour, warmed on the water-bath for 0·5 hr., diluted with water (80 c.c.), neutralised with sodium hydrogen carbonate, and extracted with ethyl acetate. Yellow needles (3·58 g.) separated from the extracts and evaporation to 50 c.c. gave a further small quantity of the same product. Recrystallisation from ethyl acetate afforded 3-*acetyl*-1-*benzyl*-5-*methoxyindole* N-*benzyl*-N-p-*methoxyphenylhydrazone* (3·61 g., 17%), m. p. 200° (Found: C, 78·3; H, 6·1; N, 8·7; OMe, 12·7. $C_{32}H_{31}N_3O_2$ requires C, 78·5; H, 6·4; N, 8·6; 2OMe, 12·7%).

Distillation of the ethyl acetate mother-liquors afforded a fraction, b. p. 138—170° (bath)/0·08 mm., which on trituration with ethanol gave *N*-benzyl-*p*-anisidine (7·47 g., 40%) as plates, m. p. and mixed m. p. 50—51° after further recrystallisation from light petroleum; the second fraction, b. p. 205—235° (bath)/0·08 mm., crystallised from methanol as needles (4·51 g., 31%) of benzaldehyde *N*-benzyl-*N*-*p*-methoxyphenylhydrazone, m. p. and mixed m. p. 119°.

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In a similar experiment with the hydrazine, acetic acid, and sodioacetylacetaldehyde in a 2 : 3 : 1 molecular ratio the yields of the indole hydrazone, the benzaldehyde hydrazone, and *N*-benzyl-*p*-anisidine, were 11, 28, and 49% respectively. In other experiments the indole hydrazone was isolated without the reaction temperature's rising above 0°.

α-*Phthalimidopropionyl Chloride.*—Equimolecular proportions of phthalic anhydride and DL-alanine were heated together at 150° until no more steam was evolved. Crystallisation of the residue from hot water gave needles, m. p. 163—164° (lit.,[30] m. p. 160—162°), of α-phthalimidopropionic acid. The latter was treated with an excess of thionyl chloride and, after being boiled under reflux during 1 hr., the solution was distilled. α-Phthalimidopropionyl chloride was collected; it had b. p. 110—113°/0·04 mm., m. p. 72—73° (lit.,[30] m. p. 73°).

Reaction of Indolylmagnesium Bromide with α-Phthalimidopropionyl Chloride.—A solution of α-phthalimidopropionyl chloride (21·83 g., 1·06 mol.) in dry ether (50 c.c.) was added dropwise to a stirred, ice-cold ethereal suspension of indolylmagnesium bromide (18·8 g., 1 mol., in 30 c.c.) at <5°. After addition of the acid chloride stirring was continued for 5 hr. and the mixture kept for 2 days at 0°. After decomposition of the red reaction complex by ice-water, and acidification, ethyl acetate extracts of the aqueous layer were combined with the ethereal layer and this solution was washed with aqueous sodium hydrogen carbonate and water, dried, and evaporated. The resultant red oil was fractionally distilled to give indole, m. p. 50—51° (5·0 g., 50% recovery), and a higher-boiling orange oil, b. p. 250—305° (bath)/0·03 mm., which crystallised from acetone–light petroleum as colourless needles of 3-α-*phthalimidopropionylindole*, m. p. 207° (0·80 g., 3% yield) (Found: C, 71·2; H, 4·3; N, 8·7. $C_{19}H_{14}N_2O_3$ requires C, 71·4; H, 4·4; N, 8·8%). The 2,4-dinitrophenylhydrazone was formed with difficulty and crystallised from benzene as orange prisms, m. p. 219—220°.

Acidification of the bicarbonate washings precipitated α-phthalimidopropionic acid, m. p. 162—163° (7·95 g., 40%).

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DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTTINGHAM.
[Present address (F. E. K.): THE BRITISH PETROLEUM COMPANY LIMITED, BRITANNIC HOUSE, FINSBURY CIRCUS, LONDON, E.C.2.] [*Received, December 20th*, 1960.]

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533. *The Chemistry of the Triterpenes and Related Compounds. Part XXXIX.* Some Derivatives of 4,4-Dimethylcholestan-3-one.*

By G. R. CHAUDHRY, T. G. HALSALL, and E. R. H. JONES.

Several 2-substituted derivatives of 4,4-dimethylcholestan-3-one have been prepared so that their properties can be compared with those of certain bitter principles which have been assigned comparable structures for ring A. The $\Delta[M]_D$ value for the conversion of 2α-hydroxy-4,4-dimethylcholestan-3-one (X) into 2-hydroxy-4,4-dimethylcholest-1-en-3-one (XI) is markedly different from the corresponding values for the conversions of cucurbitacins B (II) into E (I) and D (IV) into I (III).

STRUCTURE (IV) has been proposed [1] for cucurbitacin D (elatericin A) and structures (I), (II), and (III) then follow for the related cucurbitacins E (α-elaterin), B, and I (elatericin B). Noller, Melera, Gut, Shoolery, and Johnson [2] have criticised structure (II), pointing out that the nuclear magnetic resonance spectrum of the diosphenols prepared from dihydro- and deacetoxydihydro-cucurbitacin B indicate that $C_{(10)}$ carries a hydrogen atom and hence is not quaternary as in structure (II).

* Part XXXVIII, *J.*, 1961, 646.

[1] Lavie and Shvo, *Chem. and Ind.*, 1960, 403; Lavie, Shvo, and Gottlieb, *Tetrahedron Letters*, 1960, No. 22, 23.

[2] Noller, Melera, Gut, Shoolery, and Johnson, *Tetrahedron Letters*, 1960, No. 15, 15.

XUM

Recently we have prepared model compounds starting from 4,4-dimethylcholestan-3-one to obtain optical-rotation data for comparison with those available for the cucurbitacins described above. Our primary aim was to prepare the α-hydroxy-ketone (X) and the diosphenol (XI).

Cholest-4-en-3-one was methylated according to the method of Woodward, Patchet, Barton, Ives, and Kelly [3] to give 4,4-dimethylcholest-5-en-3-one. This was converted into the saturated ketone (V) by hydrogenation and oxidation of the resulting 4,4-dimethyl-5α-cholestan-3β-ol. Besides the 4,4-dimethyl-5α-cholestan-3β-ol the corresponding 3α-alcohol was isolated, as were also 4,4-dimethyl-5β-cholestan-3α- and -3β-ol. The last two alcohols were distinguished on the basis of their ease of elution from alumina, the more easily eluted being assumed to have an axial (3β) hydroxyl group. Oxidation of the two 4,4-dimethyl-5β-cholestan-3-ols gave 4,4-dimethyl-5β-cholestan-3-one.

The ketone (V) was treated with bromine (1·1 mol.) in acetic acid containing a little hydrobromic acid, and two crystalline monobromo-ketones, m. p.s 110—112° and 71°, were isolated. These must be epimeric at position 2. The one with m. p. 110—112° had an ultraviolet maximum at a wavelength 50 Å less than that of the parent ketone. The infrared frequency of its carbonyl group was 23 cm.$^{-1}$ greater. The corresponding figures for the bromo-ketone, m. p. 71°, were −30 Å and +20 cm.$^{-1}$. These results indicate [4,5] that in both bromo-ketones the bromine is equatorially disposed. Barton, Lewis, and McGhie,[6] and Cummins and Page,[7] have obtained similar spectroscopic results with the two epimeric 2-bromo-derivatives of lanostan-3-one and lanost-8-en-3-one. As in these cases [6] our results can be explained by assuming that we have a 2α-bromo-ketone (VI) with ring A in the chair conformation and a 2β-bromo-ketone (VII) with ring A as a boat. The $\Delta[M]_D$ for the introduction of the 2β-bromine atom in lanostan-3-one is +544° and for the 2α-bromine +69°.[6] The $\Delta[M]_D$ value for the 2-bromo-ketone, m. p. 110—112°, was +227° and for the other, m. p. 72°, was −48°, indicating that the former is the 2β-bromo-derivative (VII) and the latter the 2α-bromo-derivative (VI). These configurational assignments are supported by optical rotatory dispersion data (cf. Table) and are consistent with an analysis of these data according to the "octant rule." [8]

Compound	Amplitude *	Δ (Subst. ketone − parent ketone)
4,4-Dimethylcholestan-3-one	−11°	
2α-Bromo-4,4-dimethylcholestan-3-one	+20	+31°
2β-Bromo-4,4-dimethylcholestan-3-one	+75	+86
Lanostan-3-one	−13	
2α-Bromolanostan-3-one	+23	+36
4,4-Dimethylcholest-5-en-3-one	+62	
2α-Bromo-4,4-dimethylcholest-5-en-3-one	+60	−2
2,2-Dibromo-4,4-dimethylcholest-5-en-3-one	−118	−180
2α-Acetoxy-4,4-dimethylcholestan-3-one	+38	+49
2β-Acetoxy-4,4-dimethylcholestan-3-one	+124	+135

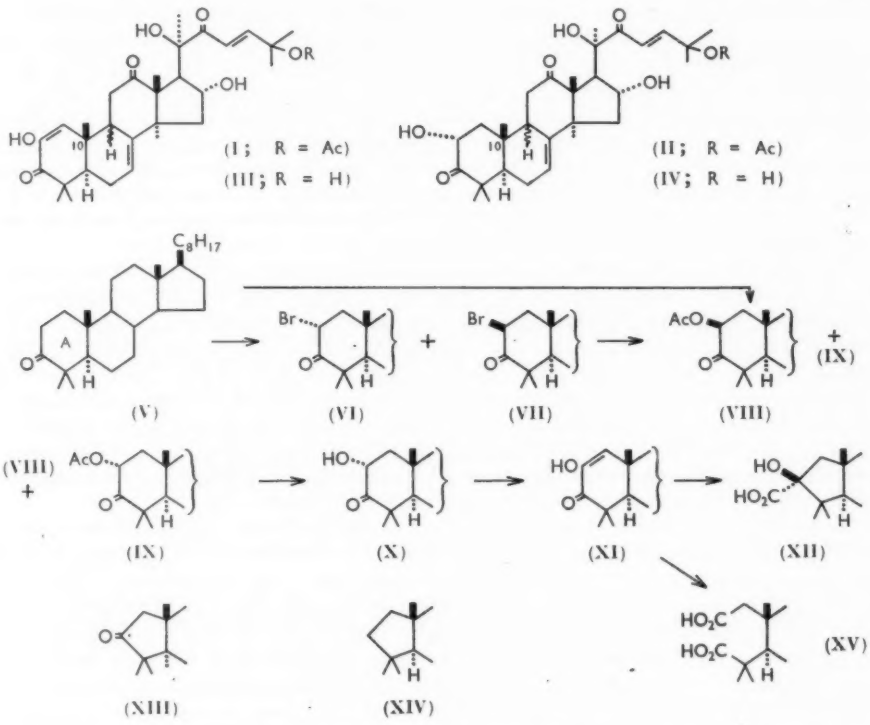
* Amplitude is the difference between the molecular rotations × 10^{-2} at the peak and trough of the Cotton curve.

Hanna, Sandris, and Ourisson [9] have also brominated 4,4-dimethylcholestan-3-one (V) but obtained only the 2,2-dibromo-derivative. The ketone has also been brominated by Sigg and Tamm [10] who obtained an amorphous monobromo-ketone, $[\alpha]_D$ +12°, which they claim is 2α-bromo-4,4-dimethylcholestan-3-one, and the 2,2-dibromo-ketone; their

[3] Woodward, Patchet, Barton, Ives, and Kelly, *J.*, 1957, 1131.
[4] Jones, Ramsey, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828.
[5] Cookson, *J.*, 1954, 282.
[6] Barton, Lewis, and McGhie, *J.*, 1957, 2907.
[7] Cummins and Page, *J.*, 1957, 3847.
[8] Moffitt, Muscovitz, Woodward, Djerassi, and Klyne, unpublished work; cf. Klyne, *J. Roy. Inst. Chem.*, 1960, **84**, 50.
[9] Hanna, Sandris, and Ourisson, *Bull. Soc. chim. France*, 1959, 1454.
[10] Sigg and Tamm, *Helv. Chim. Acta*, 1960, **43**, 1402.

constants, however, indicate that their monobromo-ketone is a mixture of *ca.* 40% of the 2β-bromo- and *ca.* 60% of the 2α-bromo-ketone.

4,4-Dimethylcholest-5-en-3-one was also brominated: the 2,2-dibromo-derivative [11] and a monobromo-derivative identical with that said [11] to be 2α-bromo-4,4-dimethylcholest-5-en-3-one were obtained. No evidence for the 2α-configuration was given. The ultraviolet maxima in both cases were at wavelengths 250 Å greater than for the parent ketone, whereas the infrared carbonyl stretching frequency was unchanged in the case of



the monobromo-ketone and only shifted by +4 cm.$^{-1}$ for the dibromo-ketone. The bromine atom in the monobromo-ketone is therefore axially disposed.[4,5] The only structure which permits the bromine atom to have an axial conformation and yet not interact with the 4- and 10-methyl groups is that with the bromine atom in the 2α-configuration and with ring A in a boat form with $C_{(1)}$ and $C_{(4)}$ at the bow and stern.

The amplitude of the Cotton effect for the monobromo-ketone is almost identical with that of the parent ketone, but uncertainty about the effect of the 5,6-double bond and the consequential flexible conformations of ring A do not allow a prediction of the configuration of the bromine atom to be made with certainty on the basis of the " octant rule." [8]

Acetoxylation of 4,4-dimethylcholestan-3-one with lead tetra-acetate in acetic acid [12] gave a mixture from which the two epimeric 2-acetates, m. p.s 115° and 147°, were isolated.

[11] Adams, Patel, Petrow, Stuart-Webb, and Sturgeon, *J.*, 1956, 4490.

[12] Cf. Ehrhart, Rushig, and Amuller, *Ber.*, 1939, **72**, 2035; Reichstein and Montigel, *Helv. Chim. Acta*, 1939, **22**, 1212; Seebeck and Reichstein, *Helv. Chim. Acta*, 1944, **27**, 948; Sondheimer, Kaufmann, Romo, Martinez, and Rosenkranz, *J. Amer. Chem Soc.*, 1953, **75**, 4712; Rosenkranz, Mancera, and Sondheimer, *J. Amer. Chem. Soc.*, 1955, **77**, 145; Clarke, Dobriner, Morradian, and Martini, *J. Amer. Chem. Soc.*, 1955, **77**, 661; Axelrod and Rao, *Chem. and Ind.*, 1959, 1454.

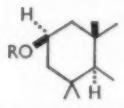
Both were also obtained by acetolysis of 2β-bromo-4,4-dimethylcholestan-3-one. The $\Delta\lambda_{max.}$ and $\Delta\nu_{max.}$ (C=O) for both compounds compared with the parent ketone were ±0 Å and +24 cm.$^{-1}$, again indicative of the equatorial conformation of the acetoxy-group in both cases. The correlation between wavelength shifts and the conformation of the acetoxy-group is, however, not always valid.[13] The acetate, m. p. 147°, shows the greater positive amplitude in its Cotton effect (cf. Table). As 2β-bromo- and 2β-methoxy-4,4-dimethylcholestan-3-one [10] show bigger positive amplitudes than the corresponding 2α-derivatives, the acetate of m. p. 147° must be 2β-acetoxycholestan-3-one (VIII) with ring A in a flexible conformation, and the acetate of m. p. 115° is the corresponding 2α-acetate (IX).

Careful hydrolysis of the 2α-acetate (IX) with alcoholic potassium hydroxide gave the 2α-hydroxy-ketone (X) as the major product, along with some of the diosphenol (XI). Hydrolysis of the 2β-acetate (VIII) also gave the 2α-hydroxy-ketone (X). This was oxidised to the diosphenol (XI) by bismuth trioxide in acetic acid (Rigby's method [14]) as well as by copper acetate in methanol.[15] This diosphenol has recently been prepared by Sigg and Tamm [10] starting from 2β-methoxy-4,4-dimethylcholestan-3-one. Its nuclear magnetic resonance spectrum was determined in chloroform. It showed a band at $\tau = 3{\cdot}6$ indicative of a β-hydrogen atom on the diosphenol group and the absence of a γ-hydrogen atom in agreement with the findings of Noller *et al.*[2]

The diosphenol (XI) underwent the benzilic acid rearrangement, which is also characteristic of ring A of cucurbitacin E (I), to give the hydroxy-acid (XII).[16] Consideration of the stereochemistry of the rearrangement indicates that attack by hydroxyl ion at either position 2 or position 3 of the diketone form of (XI) will lead to a β-orientation for the hydroxyl group of the hydroxy-acid. Fission of the hydroxy-acid (XII) with lead tetra-acetate gave the A-nor-ketone (XIII) recently described by Hanna, Sandris, and Ourisson [9] and also prepared in reasonable yield by pyrolysis, after treatment with acetic anhydride, of the *seco*-diacid (XV) obtained by oxidation of the diosphenol (XI) with alkaline hydrogen peroxide. Wolff–Kishner reduction of the A-nor-ketone gave 3,3-dimethyl-A-norcholestane (XIV). The $\Delta[M]_D$ for the reduction (−402°) is as expected.[17]

The $\Delta[M]_D$ value for the conversion of the 2α-hydroxy-ketone (X) into the diosphenol (XI) is +110° whereas the values for the conversion of cucurbitacin B (II) [18] into E (I) [19] and of cucurbitacin D (IV) [20] into I (III) [20] are −847° and −509° respectively. This very significant difference between the 4,4-dimethylcholestane derivatives and the cucurbitacins could well be due to the 7,8-double bond if structures (I—IV) are correct. It does, however, also suggest that there may be some profound difference between rings A of cucurbitacins E and I and ring A of 2-hydroxy-4,4-dimethylcholest-1-en-3-one, as is suggested in the recent paper of Noller and his co-workers.[2]

Lavie and Gottlieb [21] recently described the 2β-epimers of dihydrocucurbitacins B and D and the acetate of the second of the epimers. If structures (I—IV) are correct these 2β-epimers should have partial structure (XVI; R = H or Ac). By analogy with 2β-acetoxy-4,4-dimethylcholestan-3-one (VIII) and the related 2β-substituted 4,4-dimethylcholestan-3-ones discussed above the hydroxy- and acetoxy-groups in the 2β-epimers of dihydrocucurbitacins B and D and of dihydrocucurbitacin D 2-acetate should be equatorially disposed. The evidence of Lavie and Gottlieb [21] indicates that their conformation is axial. This conclusion again suggests the absence of a



(XVI)

[13] Elks, Phillips, Walker, and Wyman, *J.*, 1956, 4330.
[14] Rigby, *J.*, 1951, 793.
[15] Wendler, Taub, and Graber, *Tetrahedron*, 1959, **7**, 173.
[16] Lavie, *Chem. and Ind.*, 1956, 466.
[17] Klyne, *J.*, 1952, 2916.
[18] Chaudhry and Halsall, *Chem. and Ind.*, 1959, 1119.
[19] Chaudhry, D.Phil. Thesis, Oxford, 1960.
[20] Lavie and Willner, *J. Amer. Chem. Soc.*, 1958, **80**, 710.
[21] Lavie and Gottlieb, *Chem. and Ind.*, 1960, 929.

XUM

10-methyl group. Clearly an attempt to extend unsaturation to position 10 in elaterin would be of interest.

Experimental

Rotations refer to solutions in $CHCl_3$ at room temperature unless otherwise stated. M. p.s were determined on a Kofler block and are corrected. The alumina used for chromatography was alumina of activity I—II; " 5% deactivated " refers to deactivation of this alumina with 5% of 10% aqueous acetic acid. Light petroleum refers to the fraction with b. p. 40—60°. Unless otherwise stated, ultraviolet spectra were determined on ethanol solutions and infrared spectra on carbon disulphide solutions.

4,4-Dimethylcholestan-3-one (V).—Cholest-4-en-3-one was converted into 4,4-dimethylcholest-5-en-3-one essentially by the method of Woodward *et al.*[3] 4,4-Dimethylcholest-5-en-3-one (30 g.) in acetic acid (700 c.c.) was shaken with hydrogen at 80—90°/1 atm. in the presence of Adams catalyst (2 g.). Absorption of hydrogen was very slow even after the addition of more catalyst (3 g.). After 16 hr. absorption of hydrogen ceased (uptake 4·5 l.; calc., 4·25 l.). After removal of the catalyst the solution was concentrated and cooled, to give needles (15 g.), m. p. 155—156°. Extraction of the mother-liquors with benzene gave further product (13 g.). The infrared spectrum of this extract indicated that acetylation had occurred during the hydrogenation. The total hydrogenation product (28 g.) was hydrolysed with 3% methanolic potassium hydroxide (500 c.c.) under reflux for 2 hr. The product crystallised from ether–methanol to give 4,4-dimethylcholestan-3β-ol (15 g.). Concentration of the mother-liquors afforded a viscous mass (13 g.) whence chromatography gave a fraction (950 mg.), m. p. 147—150°, and a second fraction (6·5 g.). The latter fraction was separated by treatment with digitonin into 4,4-dimethylcholestan-3β-ol (5 g.) and two fractions, m. p. 44—55°, $[\alpha]_D$ +22°, and m. p. 80—95°. The two crops (20 g.) of 4,4-dimethylcholestan-3β-ol were crystallised from methylene dichloride–methanol, to give needles (18 g.), m. p. 157—158°, $[\alpha]_D$ +11° (*c*, 1·0). Mazur and Sondheimer [22] report m. p. 157—158°, $[\alpha]_D$ +11°.

The fraction, m. p. 147—150°, was adsorbed on alumina (5% deactivated). Elution with benzene gave a fraction which crystallised from ether–methanol to give *4,4-dimethylcholestan-3α-ol* as needles, m. p. 145—147°, $[\alpha]_D$ +50° (*c* 1·0), $\nu_{max.}$ 3571, 1060, and 990 cm.$^{-1}$ (Found: C, 83·3; H, 12·3. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%). Oxidation of the alcohol in acetone with 8N-chromic acid [23] gave 4,4-dimethylcholestan-3-one (see below), m. p. and mixed m. p. 103—104°, $[\alpha]_D$ +3°.

The fraction, m. p. 44—55°, $[\alpha]_D$ +22°, was adsorbed on alumina (5% deactivated). Elution with benzene gave a fraction which crystallised from ether–methanol to give *4,4-dimethyl-5β-cholestan-3β-ol* as needles, m. p. 70—72°, $[\alpha]_D$ +33° (*c* 1·0), $\nu_{max.}$ 3571, 1039, 975, and 925 cm.$^{-1}$ (Found: C, 83·55; H, 12·2. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%).. Oxidation of the alcohol in acetone with 8N-chromic acid [23] gave a product which on chromatography on alumina gave *4,4-dimethyl-5β-cholestan-3-one* as plates (from ether–methanol), m. p. 62—65°, $[\alpha]_D$ +15° (*c* 1·0), $\nu_{max.}$ 1706, 1127, and 1114 cm.$^{-1}$, $\lambda_{max.}$ 2870 Å (ε 30) (Found: C, 83·85; H, 12·1. $C_{29}H_{50}O$ requires C, 84·0; H, 12·15%). R.D. in MeOH (*c* 0·1), [*M*]: (3100 Å), −1480°; (2750 Å) +1240°.

The fraction, m. p. 80—95°, was adsorbed on alumina (5% deactivated). Elution with benzene gave material which crystallised from ether–methanol to give *4,4-dimethyl-5β-cholestan-3α-ol* as plates, m. p. 98—100°, $[\alpha]_D$ +23° (*c* 1·0), $\nu_{max.}$ 3559, 1039, 975, and 925 cm.$^{-1}$ (Found: C, 83·2; H, 12·45. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%). The alcohol was oxidised as described above to 4,4-dimethyl-5β-cholestan-3-one, m. p. and mixed m. p. 62—65°, $[\alpha]_D$ +14° (*c* 1·0).

4,4-Dimethylcholest-5-en-3-one (5 g.) was also hydrogenated at 50—60°/1 atm. in acetic acid (100 c.c.) containing 2 drops of 60% perchloric acid and Adams catalyst (1 g.). Hydrogenation was complete after 3 hr. After removal of the catalyst and concentration of the solution crystals (3·7 g.) were formed at 20°. Recrystallisation of these from methylene dichloride–methanol gave 4,4-dimethylcholestan-3β-ol as needles (3·3 g.), m. p. 157—158°, $[\alpha]_D$ +11° (*c* 1·07).

4,4-Dimethylcholestan-3β-ol (18 g.) was oxidised in acetone (1500 c.c.) with 8N-chromic

[22] Mazur and Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.
[23] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2555.

acid.[23] 4,4-Dimethylcholestan-3-one was obtained as needles (16 g.) (from methylene dichloride–methanol), m. p. 103—104°, $[\alpha]_D$ +2°. R.D. in MeOH (*c* 0·1), [*M*]: (3200 Å), −800°; (2850 Å), +300°.

Bromination of 4,4-*Dimethylcholestan*-3-*one*.—Bromine (470 mg., 1·1 mol.) in acetic acid (2 c.c.) containing 2 drops of hydrobromic acid was added in ½ hr. to a stirred solution of 4,4-dimethylcholestan-3-one (1·13 g.) in acetic acid (20 c.c.) at 20°. The stirring was continued for ½ hr. and then the solution was kept at 20° for 48 hr.; a product (300 mg.) crystallised as needles. These were isolated. The mother-liquor was diluted with water and extracted with ether. The extract (400 mg.) was dissolved in ether (5 c.c.), and the solution was diluted with ethanol (25 c.c.) and kept at 0° for several days. Further crystals (300 mg.) separated. The total crystalline product (600 mg.) was repeatedly crystallised from ether–ethanol, to give crude 2β-bromo-4,4-dimethylcholestan-3-one, m. p. 106—108°. The crude 2β-bromo-product (500 mg.) was chromatographed on silica gel (160 g.). Elution with light petroleum–benzene afforded 2β-*bromo*-4,4-*dimethylcholestan*-3-*one* (VII) (450 mg.) which crystallised from ether–ethanol as needles, m. p. 110—112°, $[\alpha]_D$ +47° (*c* 1·0), $\lambda_{max.}$ 2850 Å (ε 45), $\nu_{max.}$ 1727, 952, 757, and 714 cm.$^{-1}$ (Found: C, 70·5; H, 10·0; Br, 16·2. $C_{29}H_{49}BrO$ requires C, 70·5; H, 10·0; Br, 16·2%), R.D. in MeOH (*c* 0·1), [*M*]: (3085 Å), +4700°; (2610 Å) −2800°.

The mother-liquors left after removal of the crude 2β-bromo-4,4-dimethylcholestan-3-one for chromatography afforded the 2α-bromo-derivative which was crystallised twice from ethanol to give 2α-*bromo*-4,4-*dimethylcholestan*-3-*one* (VI) as needles, m. p. 70—71° $[\alpha]_D$ −8° (*c*, 1·0), $\lambda_{max.}$ 2870 Å (ε 30), $\nu_{max.}$ 1724, 952, and 757 cm.$^{-1}$ (Found: C, 70·5; H, 10·0; Br, 16·2%). R.D. in MeOH (*c* 0·1), [*M*]: (3375 Å) −120°; (2960 Å) +2150°.

Reduction of 2β-*Bromo*-4,4-*dimethylcholestan*-3-*one*.—This ketone (150 mg.), zinc dust (500 mg.), and acetic acid (10 c.c.) were heated at 100° for 2 hr. After filtration and dilution with water, ether-extraction afforded 4,4-dimethylcholestan-3-one (75 mg.), m. p. and mixed m. p. 103°.

Bromination of 4,4-*Dimethylcholest*-5-*en*-3-*one*.—4,4-Dimethylcholest-5-en-3-one (6·9 g.) in chloroform (60 c.c.) and acetic acid (60 c.c.) was treated at 20° during 1 hr., with stirring, with bromine (3·5 g., 1·3 mol.) in acetic acid (5 c.c.) containing 2 drops of 50% hydrobromic acid in acetic acid. The solvent was removed at 20°. The resulting crystalline product was washed with methanol (3 × 5 c.c.), affording prisms (4·5 g.). After three crystallisations from chloroform–methanol, the fraction, m. p. 135—138°, was recrystallised thrice from ethanol, to give 2α-bromo-4,4-dimethylcholest-5-en-3-one as plates (2 g.), m. p. 138—139°, $[\alpha]_D$ −28° (*c* 1·0), $\lambda_{max.}$ 3150 Å (ε 140), $\nu_{max.}$ 1724, 1105, 1026, and 769 cm.$^{-1}$ (Found: C, 70·7; H, 9·5; Br, 16·0. Calc. for $C_{29}H_{47}BrO$: C, 70·9; H, 9·6; Br, 16·3%). R.D. in MeOH (*c* 0·1), [*M*]: (3360 Å) +1300°, (2800 Å) −4750°. Adams *et al.*[11] give m. p. 136—137°, $[\alpha]_D$ −25°.

The intermediate fractions (2 g.), m. p. 80—95°, obtained during the fractional crystallisation were chromatographed on silica gel (200 g.). Light petroleum–benzene (9 : 1; 500 c.c.) eluted a fraction (700 mg.) which crystallised from chloroform–methanol to give 2,2-dibromo-4,4-dimethylcholest-5-en-3-one as rods, m. p. 94—95°, $[\alpha]_D$ −34°, $\lambda_{max.}$ 3150 Å (ε 120), $\nu_{max.}$ 1724, 1042, 1031, 952, 877, 787, and 702 cm.$^{-1}$ (Found: C, 60·8; H, 8·1; Br, 28·2. Calc. for $C_{29}H_{46}Br_2O$: C, 61·0; H, 8·1; Br, 28·1%). R.D. in MeOH (*c* 1·0), [*M*]: (3475 Å), −4050° (2975 Å), +7750°. Adams *et al.*[11] give m. p. 94—96°.

Acetolysis of 2β-*Bromo*-4,4-*dimethylcholestan*-3-*one*.—The bromo-ketone (500 mg.) in acetic acid (10 c.c.) and freshly fused potassium acetate (2·0 g.) were heated under reflux under nitrogen for 4 hr. After dilution with water, ether-extraction afforded an oil (400 mg.) which was triturated with methanol. The resulting solution was boiled with charcoal and then concentrated and kept at 0°. The crude crystalline product (200 mg.) was resolved by several crystallisations from ether–methanol into two crystalline components: (a) 2α-*acetoxy*-4,4-*dimethylcholestan*-3-*one* (IX) (50 mg.), m. p. 115°, $[\alpha]_D$ +38° (*c* 1·0), $\lambda_{max.}$ 2900 Å (ε 38), $\nu_{max.}$ 1748, 1727, 1230, 1084, 1047, and 1031 cm.$^{-1}$ (Found: C, 78·7; H, 11·0; Ac, 9·0. $C_{31}H_{52}O_3$ requires C, 78·75; H, 11·1; Ac, 9·1%) {R.D. in MeOH (*c*, 0·104). [*M*]: (3120 Å), +2140°, (2720 Å) −1640°}, and (b) 2β-*acetoxy*-4,4-*dimethylcholestan*-3-*one* (VIII) (45 mg.), m. p. 145°, $[\alpha]_D$ +59° (*c* 1·0), $\lambda_{max.}$ 2900 Å (ε 40), $\nu_{max.}$ 1748, 1727, 1227, 1084, and 1047 cm.$^{-1}$ (Found: C, 78·75; H, 11·1; Ac, 9·0%) {R.D. in MeOH (*c* 0·106), [*M*]: (3070 Å), +7050°; (2700 Å) −5400°}.

Acetoxylation of 4,4-*Dimethylcholestan*-3-*one*.—4,4-Dimethylcholestan-3-one (10 g.), lead tetra-acetate (15 g.), and acetic acid (100 c.c.) were heated for 4 hr. at 100°. Most of the solvent was removed under reduced pressure and the resulting viscous mass was macerated with water

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(300 c.c.). A sticky pale-yellow solid separated and the aqueous layer was decanted. The solid was again macerated with water (2 × 100 c.c.), and the combined aqueous washings were partially neutralised with sodium hydrogen carbonate solution and extracted with benzene. The solid was dissolved in the benzene extract which was then worked up in the usual manner, to give a residue (12 g.) which was adsorbed from light petroleum on alumina (5% deactivated) (1 kg.). The following fractions were eluted with the solvents indicated: (i) light petroleum (3 l.), 100 mg.; (ii) light petroleum–benzene (2 l.; 19 : 1) 70 mg.; (iii) light petroleum–benzene (4 l.; 9 : 1), 760 mg.; (iv) and (v) light petroleum–benzene (4 : 1), (1 l.), 130 mg., (5 l.), 805 mg.; (vi) and (vii) light petroleum–benzene (7 : 3), (1 l.), 340 mg.; (500 c.c.), 530 mg.; (viii)—(xix) light petroleum–benzene (7 : 3) (12 × 600 c.c.), 5·91 g. Fractions (i)—(vii) did not crystallise. Each of the twelve fractions (viii)—(xix) was fractionally crystallised from ether–methanol, to give crops of the two acetoxy-isomers (m. p.s 113—115° and 145—146°). The earlier fractions were richer in the lower-melting isomer, the later fractions in the higher-melting.

The fractions (2·5 g.) with m. p.s 113—115° were combined and crystallised from ether–methanol, to give 2α-acetoxy-4,4-dimethylcholestan-3-one as needles, m. p. and mixed m. p. 115°, $[\alpha]_D$ +38° (*c* 1·0). The fractions (3·0 g.) melting at 143—145° were combined and crystallised from ether–methanol, to give 2β-acetoxy-4,4-dimethylcholestan-3-one as needles, m. p. and mixed m. p. 146—147°, $[\alpha]_D$ +61°. In other experiments the proportion of the two isomers varied, but the 2β-acetoxy-isomer was always predominant.

Hydrolysis of 2α-*Acetoxy*-4,4-*dimethylcholestan*-3-*one* (IX).—The acetate (700 mg.) in ethanol (15 c.c.) was treated with M-potassium hydroxide (5 c.c.) under nitrogen. The mixture was shaken at 20° and after 10 min. the product began to be precipitated. After a further 5 min. the solution was acidified with alcoholic M-acetic acid (5 c.c.). The solvent was removed under reduced pressure and the residue was extracted with ether to give a product which contained both saturated and αβ-unsaturated ketones ($\nu_{max.}$ 3460, 1718, 1675, and 1650 cm.$^{-1}$). The mixture (520 mg.) was chromatographed on silica gel (150 g.). Light petroleum–benzene (1 : 1) eluted a product (30 mg.), m. p. 161—162° raised by crystallisation from ether–methanol to 166—167°. Its infrared spectrum ($\nu_{max.}$ 3425, 1672, and 1650 cm.$^{-1}$) indicated that it was a diosphenol. Elution with light petroleum–benzene (3 : 7; 500 c.c.) gave a product (400 mg.) which was crystallised from ether–methanol to give 2α-*hydroxy*-4,4-*dimethylcholestan*-3-*one* (X) as needles, m. p. 133—134°, $[\alpha]_D$ +24° (*c* 1·0), $\lambda_{max.}$ 2820—2830 Å (ε 41), $\nu_{max.}$ 3460, 1718, 1136, 1092, and 1056 cm.$^{-1}$ (Found: C, 80·45; H, 11·8. $C_{29}H_{50}O_2$ requires C, 80·85; H, 11·7%).

Hydrolysis of 2β-*Acetoxy*-4,4-*dimethylcholestan*-3-*one* (VIII).—The acetate (1·23 g.) was hydrolysed as described above, to give also 2α-hydroxy-4,4-dimethylcholestan-3-one (800 mg.), m. p. and mixed m. p. 133—134°, $[\alpha]_D$ +24° (*c* 1·0).

Oxidation of 2α-*Hydroxy*-4,4-*dimethylcholestan*-3-*one* (X).—The hydroxy-ketone (800 mg.) in acetic acid (15 c.c.) was heated under reflux with bismuth oxide (400 mg.) at 100° for ½ hr. More bismuth oxide (400 mg.) was added and the heating was continued for a further ½ hr. After filtration of inorganic material, the yellow filtrate was diluted with ether. A precipitate (1·8 g.) consisting of the diosphenol and bismuth acetate was obtained. It was washed with water, and the washings and the filtrate from the precipitate were extracted with benzene. The washed precipitate was dissolved in the benzene extract which was then purified in the usual manner and evaporated. The residue (600 mg.) was chromatographed on silica gel (200 g.). Light petroleum–benzene (7 : 3; 1·5 l.) eluted a product (500 mg.) which crystallised from ether–methanol to give 2-hydroxy-4,4-dimethylcholest-1-en-3-one (XI) as plates, m. p. 168°, $[\alpha]_D$ +50° (*c* 1·0), $\lambda_{max.}$ 2680—2700 Å (ε 10,650), $\lambda_{max.}$ (alcoholic alkali) 3100—3120 Å (ε 10,000), $\nu_{max.}$ 3425, 1672, 1647, 1225, and 1053 cm.$^{-1}$ (Found: C, 81·0; H, 11·2. Calc. for $C_{29}H_{48}O_2$: C, 81·25; H, 11·3%). Sigg and Tamm [10] give m. p. 165—167°, $[\alpha]_D$ +47° ± 3°., R.D. in MeOH (*c* 0·1), [*M*]: (3580 Å) −1700°; (3340 Å) ±0°; (3024 Å) +6000°.

Rearrangement of 2-*Hydroxy*-4,4-*dimethylcholest*-1-*en*-3-*one* (XI).—The diosphenol (500 mg.) in ethanol (15 c.c.) was heated under reflux with 10% alcoholic sodium hydroxide (10 c.c.) for 5 hr. Most of the ethanol was removed under reduced pressure. After dilution with water and acidification with hydrochloric acid ether-extraction afforded a solution which was extracted with 1% sodium hydrogen carbonate solution. This was acidified with hydrochloric acid and extracted with ether and ethyl acetate. The extracts afforded a residue (400 mg.) which was further purified by dissolution in 2% sodium hydrogen carbonate solution followed by filtration, acidification, and extraction. The resulting product (300 mg.) was triturated with methylene chloride and then acetone. The residue (254 mg.) crystallised from ether–methanol to give

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2β-hydroxy-3,3-dimethyl-A-norcholestane-2α-carboxylic acid (XII) as leaflets, m. p. 247—250°, $[\alpha]_D$ +21° (*c* 1·0 in pyridine), $\nu_{max.}$ 3484, 1704, 1180, 1089, 1073, 1055, and 727 cm.$^{-1}$ (Found: C, 77·65; H, 11·1. Calc. for $C_{28}H_{50}O_3$: C, 77·95; H, 11·3%). Hanna, Sandris, and Ourisson [9] give m. p. 263—265° (evacuated capillary), $[\alpha]_D$ +25° (in dioxan).

Preparation of 2β-*Hydroxy*-3,3-*dimethyl*-A-*norcholestane*-2α-*carboxylic Acid* (XII) *from* 2α- *and* 2β-*Acetoxy*-4,4-*dimethylcholestan*-3-*one*.—The 2α-acetate (1·0 g.) in 25% alcoholic potassium hydroxide (20 c.c.) was kept at 20° for 1 hr. and then heated under reflux for 5 hr. The resulting hydroxy-acid (500 mg.), m. p. 245—250°, $[\alpha]_D$ +25° (*c* 1·0 in pyridine), was then isolated in a manner similar to that described above. The acid was similarly obtained from the 2β-acetate.

3,3-*Dimethyl*-A-*norcholestan*-2-*one* (XIII).—Lead tetra-acetate (750 mg.) and 2β-hydroxy-3,3-dimethyl-A-norcholestane-2α-carboxylic acid (500 mg.) in acetic acid (20 c.c.) were heated at 100° for 4 hr. and then kept overnight at 20°. Water (25 c.c.) was added and a solid separated. It was filtered off and the filtrate extracted with benzene. The solid was dissolved in the extract which was washed with water, sodium hydrogen carbonate solution, and water, and dried. Evaporation gave a crystalline residue (350 mg.) which crystallised from ether–methanol as needles, m. p. 130—134°. These were purified by chromatography on alumina (50 g.; 5% deactivated) and then crystallised from ether–methanol to give 3,3-dimethyl-A-norcholestan-2-one as needles (250 mg.), m. p. 134°, $[\alpha]_D$ +115°, $\lambda_{max.}$ 2980 Å (ε 38), $\nu_{max.}$ 1742 cm.$^{-1}$ (Found: C, 83·75; H, 12·0. Calc. for $C_{28}H_{48}O$: C, 83·95; H, 12·1%). R.D. in MeOH (*c* 0·1), [*M*]: (3170 Å) +11,400°; (2790 Å) −10,500°. Hanna, Sandris, and Ourisson [9] give m. p. 131°, $[\alpha]_D$ +110°.

Oxidation of 2-*Hydroxy*-4,4-*dimethylcholest*-1-*en*-3-*one with Alkaline Hydrogen Peroxide*.—Hydrogen peroxide (100-vol.; 6 c.c.) and 10% potassium hydroxide (12 c.c.) were added in 3 equal portions at intervals of 15 min. to a solution of the diosphenol (700 mg.) in ethanol (25 c.c.) which was heated under reflux. After the mixture had been kept at 20° for 2 hr. it was diluted with water and extracted with ether. The aqueous portion was acidified and extracted with ether to give a crystalline residue (540 mg.) which was triturated with methylene dichloride. The insoluble acid crystallised from ether–methanol to give 4,4-*dimethyl*-2,3-*secocholestane*-2,3-*dioic acid* (XV) as leaflets, m. p. 205—207°, $\nu_{max.}$ 1724 and 1701 (sh) cm.$^{-1}$, (Found: C, 75·5; H, 10·85%; equiv., 231. $C_{29}H_{50}O_4$ requires C, 75·3; H, 10·9%; equiv., 231·5).

Pyrolysis of 4,4-*Dimethyl*-2,3-seco*cholestane*-2,3-*dioic Acid*.—The acid (350 mg.) was heated under reflux for 1 hr. in acetic anhydride. The anhydride was then distilled off and the temperature raised to 250°. When evolution of gas had ceased the residue was distilled at 280—300°/0·02 mm. The distillate (250 mg.) crystallised on cooling. It was heated under reflux under nitrogen for 30 min. with 5% alcoholic sodium hydroxide (5 c.c.). After evaporation of the ethanol, dilution with water and ether-extraction afforded a crystalline product (200 mg.). It was purified by chromatography on alumina (5% deactivated; 50 g.) and crystallised from ether–methanol to give 3,3-dimethyl-A-norcholestan-2-one as needles, m. p. and mixed m. p. 134°.

Wolff–Kishner Reduction of 3,3-*Dimethyl*-A-*norcholestan*-2-*one*.—The ketone (250 mg.) was heated under reflux under nitrogen with diethylene glycol (40 c.c.) and 100% hydrazine hydrate (2·5 c.c.) for 2 hr. The excess of hydrazine and water were removed by distillation, potassium hydroxide (600 mg.) was added, and the mixture was heated at 210—220° for 6 hr. After dilution with water, ether-extraction afforded a liquid (200 mg.) which was adsorbed from light petroleum on alumina (15 g.). Elution with light petroleum (200 c.c.) gave 3,3-*dimethyl*-A-*norcholestane* (XIV) which crystallised from acetone as needles, m. p. 99—100°, $[\alpha]_D$ +15°, no carbonyl band in the infrared spectrum (Found: C, 86·6; H, 13·0. $C_{28}H_{50}$ requires C, 87·0; H, 13·0%). R.D. in MeOH (*c* 0·1), [*M*]: (5000 Å) +75°, (4000 Å) +287°, (3000 Å) +600°; plain positive curve.

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THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, December 22nd*, 1960.]

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534. *The Preparation and Some Reactions of 4-Formyl-1-phenylpyrazoles.*

By I. L. Finar and M. Manning.

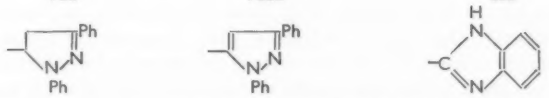
Various pyrazoles have been formylated, and in each case there has been isolated an intermediate, the composition of which supports the mechanism of formylation proposed by Smith [1] and Silverstein *et al.*[2] The aldehydes have been oxidised to the corresponding acids and the influence of alkyl and aryl substituents on the reactivity of the aldehydic group has been investigated in a series of condensations with aniline, malonic acid, acetophenone, and *o*-phenylenediamine. Six bipyrazolyls have also been prepared.

Phosphoryl chloride and dimethylformamide have been used by Finar and Lord to formylate 1-phenylpyrazole,[3a] 1-methylpyrazole,[3a] and 1,1′,3-triphenyl-4′,5-bipyrazolyl [3b] in the 4-position. Formylations have now been carried out with the substituted pyrazoles (I; $R^2 = H$, i—vi) to give the pyrazole-4-aldehydes (II; $R^2 = CHO$, i—vi). There is a slight decrease in yield with increasing size of substituent (Table 1).

I; $R^2 = H$	i	ii	iii	iv	v	vi
R^1	Me	H	Me	Me	Ph	Ph
R^3	H	Me	Me	Ph	Me	Ph

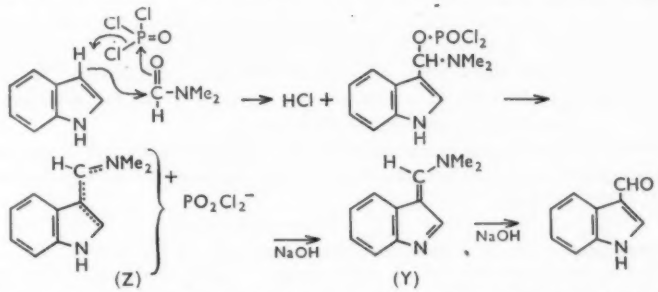
I	II	III	IV	V	VI
$R^2 = H$	CHO	CO_2H	$CH{=}CH{\cdot}CO_2H$	$CH{=}NPh$	$CH{=}CH{\cdot}COPh$

VII VIII IX



Smith,[1] who studied the formylation of indole with phosphoryl chloride and dimethylformamide, believed that the reaction proceeded through the mesomeric cation (Z) as intermediate which, on hydrolysis, gives 3-formylindole. He proposed the mechanism (A). This was supported by the isolation of the free base (Y). Silverstein *et al.*,[2] investigating

Scheme (A)



the formylation of pyrroles, proposed an attack by the initial 1 : 1 phosphoryl chloride–dimethylformamide complex at position 2 of the pyrrole nucleus, to give the intermediate (X), which is hydrolysed to the aldehyde (scheme B). Bosshard and Zollinger [4] prepared this 1 : 1 complex and showed that it formylated *NN*-dimethylaniline.

[1] Smith, *J.*, 1954, 3842.
[2] Silverstein, Ryskiewicz, Willard, and Koehler, *J. Org. Chem.*, 1955, **20**, 668.
[3] Finar and Lord, (*a*) *J.*, 1957, **3314**; (*b*) *J.*, 1959, **1819**.
[4] Bosshard and Zollinger, *Helv. Chim. Acta*, 1959, **42**, 1659.

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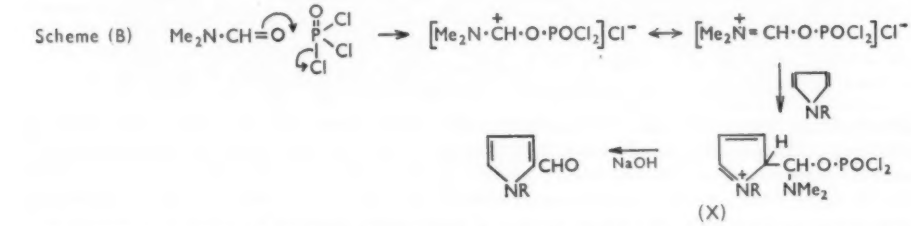
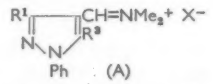
The present work has resulted in the isolation of the cation (corresponding to Z), as the dichlorophosphate or hexachloroplatinate (Table 2). Chlorine and phosphorus analyses are in agreement with the general structure (A*a*) where $X = PO_2Cl_2$, for the six substituted pyrazolyl intermediates. On the other hand, the intermediate obtained in the formylation of 1-phenylpyrazole was shown to have structure (A*b*), where X = Cl. These intermediates (A*a*, i-vi; and A*b*, vii) were obtained by triturating the reaction mixture

Scheme (B)



with either absolute alcohol or dry propanol, cooled to about −80°, and washing the precipitate with ether.



	a	*b*	*c*
X =	PO_2Cl_2	Cl	$\frac{1}{2}PtCl_6$

The intermediates dissolve readily in water and liberate the respective aldehydes when these solutions are kept. Dimethylamine hydrochloride was isolated from each intermediate by precipitation with dry ether from cooled, previously refluxed ethanolic solutions.

Further evidence for the ionic nature of the intermediates was as follows. Precipitates were obtained by treating the aqueous solutions with aqueous chloroplatinic acid, picric acid, or sodium tetraphenylborate. Estimation of chlorine in the chloroplatinates agreed with the structures (A*c*). The quantitative formation of the picrate [A*d*; $X = O{\cdot}C_6H_2(NO_2)_3$] and the tetraphenylborate (A*e*; $X = BPh_4$) from some of these intermediates supports their structures.

The substituted formyl compounds, on oxidation, gave the corresponding carboxylic acids (III; Table 3). These formyl compounds also condensed with malonic acid [5] to form β-1-phenyl-4-pyrazolylacrylic acids (IV; Table 4).

Only the 3- and the 5-methyl-1-phenylpyrazole-aldehydes formed anils [6] (V) under the conditions used. Ketones (VI; Table 5) were prepared by condensing the aldehydes with acetophenone and these were condensed with phenylhydrazine to give the pyrazolines (VII; Table 6). All the pyrazolines were oxidised to the corresponding pyrazoles (VIII; Table 7) by potassium permanganate in pyridine.

4-Formyl-1-phenylpyrazole and the six substituted formyl compounds have also been condensed with *o*-phenylenediamine,[7] giving the corresponding 2-pyrazol-4′-ylbenzimidazoles (IX; Table 8).

Experimental

Preparation of the 1-(*Substituted Phenyl*)*pyrazoles*.—Pyrazoles (I; $R^3 = H$; i[8], ii[8], iii[9], iv[10], v[11], vi[12], vii[13]) were prepared by condensation of phenylhydrazine with the appropriate β-diketone in glacial acetic acid.

[5] Finar and Godfrey, *J.*, 1954, 2293.
[6] Finar and Utting, *J.*, 1959, 4015.
[7] Weidenhagen, *Ber.*, 1936, **69**, 2263.
[8] Finar and Hurlock, *J.*, 1958, 3259.
[9] Knorr, *Ber.*, 1887, **20**, 1103.
[10] Drumm, *Proc. Roy. Irish Acad.*, 1931, **40**, *B*, 106.
[11] Minunni, Lazzarini, and d'Urso, *Gazzetta*, 1925, **55**, 502.
[12] Knorr and Laubmann, *Ber.*, 1888, **21**, 1205.
[13] Finar and Hurlock, *J.*, 1957, 3024.

Formylation to yield the Pyrazole-4-aldehydes [3] (II).—To a stirred mixture of 3-methyl-1,5-diphenylpyrazole (23·4 g., 0·1 mole) and dimethylformamide (14·6 g., 0·2 mole) at 95—100° was added phosphoryl chloride (19·4 g., 0·125 mole) dropwise during 45 min. Heating and stirring were maintained for a further 2 hr. The mixture was cooled to 0°, the pH adjusted to 4—6 by addition of aqueous sodium hydroxide, and after 6 hr. the aldehyde was collected and recrystallised twice from ethanol to give colourless prisms of *4-formyl-3-methyl-1,5-diphenylpyrazole* (62%), m. p. 136—137° (Found: C, 78·0; H, 5·4; N, 10·5. $C_{17}H_{14}N_2O$ requires C, 77·9; H, 5·3; N, 10·7%).

The other formyl derivatives were prepared in a similar manner (Table 1).

TABLE 1. *4-Formyl-1-phenylpyrazoles* (II; R^2 = CHO).

				Yield	Found (%)				Required (%)		
No.	R^1	R^3	M. p.	(%)	C	H	N	Formula	C	H	N
i	Me	H	60—61° [a]	74	71·1	5·4	15·1	$C_{11}H_{10}N_2O$	71·1	5·4	15·1
ii [d]	H	Me	75·5—76·5 [b]	75							
iii [d]	Me	Me	123—124 [a]	70							
v [d]	Ph	Me	101—101·5 [a]	63							
vi	Ph	Ph	160·5—161·5 [c]	57	81·5	5·1	8·6	$C_{22}H_{16}N_2O$	81·5	4·9	8·6

[a, b, c] Recrystallised from (*a*) aqueous ethanol, (*b*) ligroin, and (*c*) aqueous acetic acid. [d] Rojahn and Farr, *Annalen*, 1923, **434**, 261.

Formylation to Isolate the Intermediates (Aa) *and* (Ab) (Table 2).—(1) *As solids.* To 3-methyl-1-phenylpyrazole (15·8 g., 0·1 mole) and dimethylformamide (14·6 g., 0·2 mole), stirred at 70—80°, was added phosphoryl chloride (19·4 g., 0·125 mole) dropwise during 30 min. Heating and stirring were continued for a further 1 hr. The solid product obtained on gradual cooling to room temperature was brought to −30° and triturated with absolute ethanol (40 c.c.) cooled to −80° and collected under anhydrous conditions. It was further washed with cooled absolute ethanol and washed well with dry ether to give, after drying *in vacuo* over phosphorus pentoxide, colourless crystals of the *salt* (A*a* i) (26 g.), m. p. 172—173° (Table 2).

Similarly were obtained the *salts* (A*a* ii) and (A*b* vii) (Table 2).

(2) *As oils.* 3-Methyl-1,5-diphenylpyrazole was formylated as in (1) above. A portion of the viscous product was cooled to −30° and dissolved in a minimum amount of absolute ethanol (cooled to −80°). An excess of dry ether was added and the precipitated oil collected by decantation. The process was repeated on the oil until the final dry ethereal washings became colourless. After drying overnight *in vacuo* over phosphorus pentoxide the red oily *dichlorodioxophosphate* (A*a* iv) was analysed for chlorine and phosphorus (Table 2).

Similarly were obtained the *salts* (A*a* iii), (A*a* v), and (A*a* vi) (Table 2).

TABLE 2. *NN-Dimethyl-N-(1-phenylpyrazol-4-ylmethylene)immonium chlorides and dichlorodioxophosphates and the corresponding hexachloroplatinates* B_2PtCl_6 (A).

			Compound			Found (%)		Required (%)	
No.	R^1	R^3	(A)	Formula	M. p.	Cl	P	Cl	P
			b [1, 2]	$C_{12}H_{14}ClN_2$	85—86 [6]	15·0	—	15·1	—
—	H	H	*c* [3]	$C_{24}H_{28}Cl_6N_6Pt$	228 *	26·3	—	26·3	—
			a [1, 3]	$C_{12}H_{16}Cl_2N_3O_2P$	172—173 [6]	20·4	8·8	20·4	8·9
i	Me	H	*c* [3]	$C_{26}H_{32}Cl_6N_6Pt$	240—242	25·3	—	25·4	—
			a [3, 4]	$C_{13}H_{16}Cl_2N_3O_2P$	118—119 [7]	20·1	8·6	20·4	8·9
ii	H	Me	*c* [3]	$C_{26}H_{32}Cl_6N_6Pt$	207—209 *	25·1	—	25·4	—
			a [3]	$C_{14}H_{18}Cl_2N_3O_2P$	Oil	19·8	8·2	19·6	8·6
iii	Me	Me	*c*	—	—	—	—	—	—
			a [3, 5]	$C_{19}H_{20}Cl_2N_3O_2P$	Oil	16·4	7·2	16·7	7·3
iv	Me	Ph	*c* [3]	$C_{38}H_{40}Cl_6N_6Pt$	201—203 *	21·4	—	21·5	—
			a [3, 5]	$C_{19}H_{20}Cl_2N_3O_2P$	Oil	16·5	7·0	16·7	7·3
v	Ph	Me	*c* [3]	$C_{38}H_{40}Cl_6N_6Pt$	215—217 *	21·2	—	21·5	—
			a [3, 5]	$C_{24}H_{22}Cl_2N_3O_2P$	Oil	14·4	6·1	14·6	6·4
vi	Ph	Ph	*c* [3]	$C_{48}H_{44}Cl_6N_6Pt$	170 *	18·8	—	19·1	—

* With decomp. [1] Chloroplatinic acid, picric acid, and sodium tetraphenylborate gave quantitative precipitates. [2] Unstable *in vacuo*. [3] Stable *in vacuo*. [4] Picrate and tetraphenylborate unstable *in vacuo*. [5] The reagents of note (1) gave oily precipitates. [6, 7] Triturating solvents were (6) propanol at −80° and (7) ethanol at −80°.

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Isolation of Dimethylamine Hydrochloride.—Solutions of the reaction intermediates (A*a*) or (A*b*) in absolute ethanol, when refluxed for 30 min. and then cooled to −80° and treated with an excess of dry cooled ether, deposited dimethylamine hydrochloride, m. p. 174—175°.

Oxidations to the Carboxylic Acids (III).—(*a*) The aldehydes (II; R^3 = CHO; i—v) were oxidised by refluxing, aqueous, alkaline potassium permanganate. The corresponding *4-carboxylic acid* was obtained in each case (Table 3). All the acids were recrystallised from aqueous ethanol.

(*b*) A pyridine solution of 4-formyl-1,3,5-triphenylpyrazole was refluxed with alkaline potassium permanganate for 20 min. Working up gave 1,3,5-triphenylpyrazole-4-carboxylic acid [14] (73%), m. p. 238—239°.

TABLE 3. *1-Phenylpyrazole-4-carboxylic acids* (III).

No.	R^1	R^3	M. p.	Yield (%)
i [a]	Me	H	196—197°	94
ii [a]	H	Me	166—167	82
iii [b]	Me	Me	200—201	90
iv [b]	Ph	Ph	205—206	87
v [c]	Ph	Me	193—194	85

[a] Bulow, *Ber.*, 1900, **33**, 3269. [b] Knorr and Blank, *Ber.*, 1885, **18**, 312. [c] *Idem, ibid.*, p. 933.

Knoevenagel Reaction,[5] *yielding Acrylic Acids* (IV).—4-Formyl-3-methyl-1,5-diphenylpyrazole (2·62 g., 0·01 mole) and malonic acid (2·08 g., 0·02 mole) were warmed on a steam-bath with pyridine (6 c.c.) and piperidine (13 drops) for 2 hr., then refluxed for 2 hr., poured on ice, and basified with sodium hydroxide. Unchanged aldehyde was collected (0·8 g.). The aqueous filtrate was extracted with ether (2 × 100 c.c.) and acidified, and the precipitate was collected and recrystallised twice from aqueous acetic acid to give colourless prisms of β-(*3-methyl-1,5-diphenylpyrazol-4-yl)acrylic acid* (2·1 g., 69%), m. p. 245—246° (Found: C, 75·1; H, 5·2; N, 9·2. $C_{19}H_{16}N_2O_2$ requires C, 75·0; H, 5·3; N, 9·2%).

The other *acrylic acids* were obtained in a similar manner (Table 4).

TABLE 4. β-(*1-Phenylpyrazol-4-yl)acrylic acids* (IV).

				Yield	Found (%)				Required (%)		
No.	R^1	R^3	M. p.	(%)	C	H	N	Formula	C	H	N
i	Me	H	166·5—167° [a]	88	68·6	5·4	12·0	$C_{13}H_{12}N_2O_2$	68·4	5·3	12·3
ii	H	Me	199—200 [a]	88	68·3	5·4	12·1	$C_{13}H_{12}N_2O_2$	68·4	5·3	12·3
iii	Me	Me	163—164 [a]	66	69·6	8·1	16·4	$C_{14}H_{14}N_2O_2$	69·4	8·3	16·6
v	Ph	Me	211·5—212·5 [a]	43	75·1	5·1	9·1	$C_{19}H_{16}N_2O_2$	75·0	5·3	9·2
vi	Ph	Ph	246—247·5 [b]	30	78·4	4·9	7·6	$C_{24}H_{18}N_2O_2$	78·7	4·9	7·6

[a, b] Recrystallised from (*a*) aqueous ethanol and (*b*) aqueous acetic acid.

Preparation of Anils [6] (V).—4-Formyl-5-methyl-1-phenylpyrazole (3·72 g., 0·02 mole) and aniline (1·8 g., 0·02 mole) in absolute ethanol (20 c.c.) were warmed on a steam-bath for 30 min., then cooled, and the precipitate was recrystallised twice from ethanol to give N-(*5-methyl-1-phenyl-4-pyrazolylmethylidene)aniline*, as white leaflets (5·0 g., 95%), m. p. 108·5—109·5° (Found: C, 78·1; H, 6·0; N, 16·0. $C_{17}H_{15}N_3$ requires C, 78·2; H, 5·7; N, 16·1%).

In the same way was obtained N-(*3-methyl-1-phenyl-4-pyrazolylmethylidene)aniline* from methanol as rhombs (92%), m. p. 75·5—76·5° (Found: C, 78·1; H, 5·5; N, 16·2. $C_{17}H_{15}N_3$ requires C, 78·2; H, 5·7; N, 16·1%).

Preparation of Acrylophenones [3b] (VI).—(1) 4-Formyl-3-methyl-1-phenylpyrazole (5·58 g., 0·03 mole) in ethanol (60 c.c.) was added dropwise with stirring to a cooled solution of sodium hydroxide (3·6 g., 0·09 mole) in water (25 c.c.), ethanol (10 c.c.), and acetophenone (3·6 g., 0·03 mole) at 0—10°. The mixture was stored for 12 hr. and the solid then collected, washed with water, and recrystallised twice from aqueous ethanol, to give needles of β-(*3-methyl-1-phenylpyrazol-4-yl)acrylophenone* (7·1 g., 82%), m. p. 137—137·5° (Found: C, 79·1; H, 5·6; N, 9·4. $C_{19}H_{16}N_2O$ requires C, 79·2; H, 5·6; N, 9·7%).

The ketones (ii—v) (Table 5) were obtained in a similar manner.

[14] Seidel, *J. prakt. Chem.*, 1898, **58**, 153.

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TABLE 5. β-(1-*Phenylpyrazol-4-yl*)*acrylophenones* (VI).

				Yield	Found (%)				Required (%)		
No.	R^1	R^3	M. p.	(%)	C	H	N	Formula	C	H	N
ii	H	Me	110·5—111°	88	79·5	5·7	9·5	$C_{19}H_{16}N_2O$	79·2	5·6	9·7
iii	Me	Me	102—102·5	96	79·7	6·1	9·2	$C_{20}H_{18}N_2O$	79·5	6·0	9·4
iv	Me	Ph	169—170	88	82·4	5·6	7·9	$C_{25}H_{20}N_2O$	82·7	5·5	7·7
v	Ph	Me	139·5—140·5	98	82·6	5·6	7·8	$C_{25}H_{20}N_2O$	82·7	5·5	7·7

(2) Because of the insolubility of 4-formyl-1,3,5-triphenylpyrazole in ethanol the acrylophenone was prepared as follows. The aldehyde (3·24 g., 0·01 mole) and absolute ethanol (100 c.c.) were placed in a stout-walled conical flask. A cooled solution of sodium hydroxide (1·2 g., 0·03 mole in 15 c.c. of water) and acetophenone (1·2 g., 0·01 mole) were then added and the stoppered flask agitated for 40 hr. The flocculent white product was collected, washed with water, and recrystallised twice from ethanol, to give light green needles of β-(1,3,5-*triphenylpyrazol-4-yl*)*acrylophenone* (3·8 g., 89·2%), m. p. 185·5—186° (Found: C, 84·5; H, 5·0; N, 6·6. $C_{30}H_{22}N_2O$ requires C, 84·5; H, 5·2; N, 6·6%).

Preparation of Pyrazolylpyrazolines (VII).—Phenylhydrazine (2·2 g., 0·02 mole) in glacial acetic acid (15 c.c.) was added quickly to a hot solution of β-(3,5-dimethyl-1-phenylpyrazol-4-yl)acrylophenone (6·04 g., 0·02 mole) in absolute ethanol (100 c.c.). The mixture was heated for 1 hr. on a steam-bath. The crystals which separated were collected, washed with a little aqueous ethanol, and recrystallised twice from aqueous ethanol, to give green needles of 5-(3,5-*dimethylpyrazol-4-yl*)-1,3-*diphenyl-2-pyrazoline* (6·2 g., 79%), m. p. 126·5—127·5° (Found: C, 79·5; H, 6·4; N, 13·9. $C_{26}H_{24}N_4$ requires C, 79·6; H, 6·1; N, 14·1%).

The other *pyrazolines* were obtained in a similar manner (Table 6). All six gave the Knorr pyrazoline test and all showed a blue fluorescence under ultraviolet light.

TABLE 6. 1,5-*Diphenyl*-5-(*pyrazol-4-yl*)-2-*pyrazolines* (VII).

				Yield	Found (%)				Required (%)		
No.	R^1	R^3	M. p.	(%)	C	H	N	Formula	C	H	N
i	Me	H	135—136° [a]	76	79·6	5·8	14·6	$C_{25}H_{22}N_4$	79·4	5·8	14·8
ii	H	Me	132—133 [a]	79	79·6	5·6	14·6	$C_{25}H_{22}N_4$	79·4	5·8	14·8
iv	Me	Ph	190—191 [a]	75	82·0	6·0	11·9	$C_{31}H_{26}N_4$	82·1	5·7	12·1
v	Ph	Me	184—185 [a]	84	81·9	5·9	11·9	$C_{31}H_{26}N_4$	82·1	5·7	12·1
vi	Ph	Ph	212—213 [b]	62	83·4	5·3	10·9	$C_{36}H_{28}N_4$	83·7	5·4	10·9

[a] Recrystallised from aqueous ethanol. [b] Purified by trituration with boiling ethanol.

Preparation of Bipyrazolyls (VIII).—A mixture of 5-(3,5-dimethylpyrazol-4-yl)-1,3-diphenyl-2-pyrazoline (1 g.), powdered potassium permanganate (1·5 g.), pyridine (15 c.c.), and water (5 c.c.) was kept at room temperature for 30 min., then refluxed for 15 min. The product recrystallised from ethanol to give colourless rhombs of 3,5-*dimethyl*-1,1′,3′-*triphenyl*-4,5′-*bipyrazolyl* (98%), m. p. 169—170° (Found: C, 79·9; H, 5·7; N, 14·5. $C_{26}H_{22}N_4$ requires C, 80·0; H, 5·6; N, 14·4%).

The other *bipyrazolyls* were obtained in a similar manner (Table 7).

TABLE 7. 1,1′,3′-*Triphenyl*-4,5′-*bipyrazolyls* (VIII).

				Yield	Found (%)				Required (%)		
No.	R^1	R^3	M. p.	(%)	C	H	N	Formula	C	H	N
i	Me	H	101·5—102·5° [a]	98	79·6	5·3	14·6	$C_{25}H_{20}N_4$	79·9	5·3	14·9
ii	H	Me	123—124 [b]	98	79·7	5·4	15·0	$C_{25}H_{20}N_4$	79·9	5·3	14·9
iv	Me	Ph	176—177 [b]	98	82·3	5·4	12·2	$C_{31}H_{24}N_4$	82·3	5·3	12·4
v	Ph	Me	193—194 [b]	95	82·1	5·1	12·2	$C_{31}H_{24}N_4$	82·3	5·3	12·4
vi	Ph	Ph	175—176 [b]	95	84·3	5·1	10·9	$C_{36}H_{28}N_4$	84·1	5·1	10·9

[a, b] Recrystallised from (*a*) aqueous methanol and (*b*) aqueous ethanol.

Preparation of Benzimidazoles [7] (IX).—To a solution of *o*-phenylenediamine (1·08 g., 0·01 mole) and cupric acetate monohydrate (4 g., 0·02 mole) in water (30 c.c.) was added 4-formyl-3-methyl-1-phenylpyrazole (1·86 g., 0·01 mole) in warm ethanol (20 c.c.), and the mixture was heated slowly on a steam-bath. The cuprous salt soon began to separate and when the solution had completely lost its blue colour it was cooled and the precipitate was collected and

decomposed in hot ethanolic suspension with hydrogen sulphide. The filtrate was boiled (to remove hydrogen sulphide), then cooled and the precipitate collected to give, after two recrystallisations from aqueous ethanol, white plates of 2-(3-*methyl*-1-*phenylpyrazol*-4-*yl*)-*benzimidazole* (2·2 g., 80%), m. p. 236·5—237·5° (Found: C, 74·6; H, 5·1; N, 20·3. $C_{17}H_{14}N_4$ requires C, 74·5; H, 5·1; N, 20·4%).

The other benzimidazoles were prepared in a similar manner (Table 8).

TABLE 8. 2-(1-*Phenylpyrazol*-4-*yl*)*benzimidazoles* (IX).

				Yield	Found (%)				Required (%)		
No.	R^1	R^3	M. p.	(%)	C	H	N	Formula	C	H	N
ii	H	Me	202—203°	84	74·6	5·1	20·1	$C_{17}H_{14}N_4$	74·5	5·1	20·4
iii	Me	Me	264—265	76	74·8	5·6	19·2	$C_{18}H_{16}N_4$	75·0	5·6	19·4
iv	Me	Ph	213—214	70	78·7	5·2	15·9	$C_{23}H_{18}N_4$	78·9	5·1	16·0
v	Ph	Me	247—248	75	78·7	5·1	16·0	$C_{23}H_{18}N_4$	78·9	5·1	16·0
vi	Ph	Ph	288—289	49	81·7	4·7	13·5	$C_{28}H_{20}N_4$	81·6	4·9	13·6
vii	H	H	249—250	90	73·6	4·6	21·2	$C_{16}H_{12}N_4$	73·8	4·6	21·5

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535. *Transition-metal Fluorocarbon Complexes. Part I. Derivatives of Perfluoro-olefins.*

By H. H. HOEHN, L. PRATT, K. F. WATTERSON, and G. WILKINSON.

The interaction of tri-iron dodecacarbonyl, $Fe_3(CO)_{12}$, with octafluorocyclohexa-1,3- or -1,4-diene forms a compound $C_6F_8Fe(CO)_3$ which must be formulated as a π-bonded olefin complex. In contrast, the interaction of tetrafluoroethylene with $Fe_3(CO)_{12}$ gives a compound $C_4F_8Fe(CO)_4$ in which the iron atom is bound to carbon by σ-bonds in a perfluorocycloalkane ring. Infrared, high-resolution nuclear magnetic resonance, and mass-spectroscopic studies support these formulations.

Products from the interaction of tetrafluoroethylene with $Co_2(CO)_8$ and $(\pi\text{-}C_5H_5)_3Co$ and of the latter with trifluoroiodomethane are described.

ALTHOUGH a very large number of olefin complexes of transition metals are known, no halogenated olefin complexes have been characterised and the interaction of chlorinated olefins with transition-metal carbonyls, a successful preparative method for hydrocarbon complexes, results in chlorination to give the metal chloride. A similar reaction to give the metal fluoride appeared to be less likely with fluorinated olefins. Further, since Dewar's view of the bonding of olefins to transition metals would imply stronger acceptor behaviour of the carbon anti-bonding π-orbitals for electron density in filled metal orbitals than for the hydrocarbons, we have studied the interactions of several fluoro-olefins with metal carbonyls.

The iron carbonyl complex isolated from the reaction products of tetrafluoroethylene with tri-iron dodecacarbonyl, $Fe_3(CO)_{12}$, was first believed [1a] to be an olefin derivative, but further work [1b] has shown that it is a cyclic perfluoroalkyl compound, $C_4F_8Fe(CO)_4$. The interaction of octafluorocyclohexa-1,3- or -1,4-dienes and $Fe_3(CO)_{12}$ gives $C_6F_8Fe(CO)_3$,[1a] which we have now shown to be the first true perfluoro-olefin–metal complex. At the present time we have failed to obtain isolable complexes from the reactions of tetrafluoroethylene and octafluorocyclohexadiene with the compounds $Mo(CO)_6$, $Mn_2(CO)_{10}$, $HMn(CO)_5$, $Ni(CO)_4$, $(\pi\text{-}C_5H_5)_2Ni$, $\pi\text{-}C_5H_5Co(CO)_2$ at temperatures up to 150°, or from these metal compounds or iron carbonyls with perfluorocyclohexene, trifluoroethylene, 1,2-difluorethylene, or perfluoro-propene or -buta-1,3-diene, although some rather air-sensitive products are formed from the perfluorobutadiene with iron and cobalt carbonyls.

[1] Watterson and Wilkinson, *Chem. and Ind.*, (*a*) 1959, 991; (*b*) 1960, 1358.

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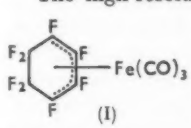
The extension of these studies to fluorinated acetylene derivatives has allowed several complexes, *e.g.*, $C_4F_6Co_2(CO)_6$, to be obtained.[2]

Octafluorocyclohexa-1,3-dieneiron Tricarbonyl.—From the products of the reaction of octafluorocyclohexa-1,3- or 1,4-diene with tri-iron dodecacarbonyl, can be readily isolated the same colourless crystalline compound, $C_6F_8Fe(CO)_3$. The spectroscopic evidence shows that in the iron compound the bound olefin is the 1,3-diene, so that the formation of the compound from the 1,4-diene must involve migration of fluorine. Examination of the surplus diene from the reaction with the 1,3- or 1,4-diene by infrared spectroscopy showed a strong absorption band at 1536 cm.$^{-1}$ which is characteristic of hexafluorobenzene; iron pentacarbonyl is also present. It was not possible to detect the 1,3-diene in surplus from the 1,4-diene reaction either spectroscopically or by vapour-phase chromatography.

The iron compound—which is volatile, subliming readily at room temperature in a vacuum, and is soluble in common organic solvents—is stable in air in the solid state indefinitely but decomposes within a few hours in cold solutions or quite rapidly in boiling benzene even in absence of air. Since conventional molecular-weight procedures (cryoscopic, ebullioscopic or isopiestic) gave obviously unreliable results, the stoicheiometry and molecular weight have been obtained by other methods. Mass-spectroscopic measurements show that the ion of greatest mass, 364, is due to $C_6F_8Fe(CO)_3^+$, while molecular-weight determination by the *X*-ray method gives a value of 361 ($\pm 2\%$). In addition, measurements of the relative peak areas in the high-resolution fluorine nuclear magnetic resonance spectrum of a known weight of the compound compared with a known weight of benzotrifluoride in acetone were taken; if eight fluorine atoms are assumed per molecule of the iron compound, the ratio of the integrated peak areas gave a molecular weight = 370 ± 5.

Infrared and nuclear magnetic resonance spectra. The infrared spectrum of $C_6F_8Fe(CO)_3$ is given in detail in the Experimental section; few assignments are possible except for the three strong carbonyl stretching frequencies at 2108, 2054, and 2018 cm.$^{-1}$, which are displaced to higher wavenumbers than in the carbonyls or the hydrocarbon complex, presumably owing to the electronegativity of the fluorine atoms which would tend to have a similar effect to that of placing a positive charge on a carbonyl complex in reducing the multiple-bond contribution in the metal–carbon bond of the M–C–O group.[3] The only other useful piece of information concerns the strong band at 1550 cm.$^{-1}$, which can be assigned as a C=C stretching frequency associated with a conjugated double-bond system. Hexafluorobenzene has an absorption at 1536 cm.$^{-1}$;[4] octafluorocyclohexa-1,4-diene absorbs at 1740 cm.$^{-1}$, and the 1,3-diene at 1750 and 1710 cm.$^{-1}$, the two bands for the latter arising from splittings due to conjugation. Since the fluoroalkyl–metal derivatives discussed below do not show a band in this region, the presence of a co-ordinated conjugated diene system seems a reasonable assumption and the downward shift of *ca.* 200 cm.$^{-1}$ is in the direction to be expected for the effect of co-ordination to the metal atom.

The high-resolution fluorine nuclear magnetic resonance spectra (at 56·45 Mc./sec.) for the iron compound and also for the two dienes are shown in the Figure; the details of the spectra and assignments are listed in the Experimental section. The spectrum of the iron compound is consistent with a structure based on a co-ordinated 1,3-diene group (I), but a similar structure with two Fe–C σ-bonds plus a co-ordinated double bond cannot be rigorously excluded.



(I)

As in the parent 1,3-diene, the pentuplet band (intensity *ca.* 2) at the highest field can be assigned to the terminal co-ordinated olefinic fluorine atoms (F_1 and F_4) and the " triplet " band (intensity *ca.* 2) next to this represents the central (F_2, F_3) olefinic fluorine atoms. The component structure is produced by spin-coupling between non-equivalent

[2] Boston, Sharp, and Wilkinson, *Chem. and Ind.*, 1960, 1137.
[3] Abel, Bennett, and Wilkinson, *J.*, 1959, 2323.
[4] Birchall and Haszeldine, *J.*, 1959, 13.

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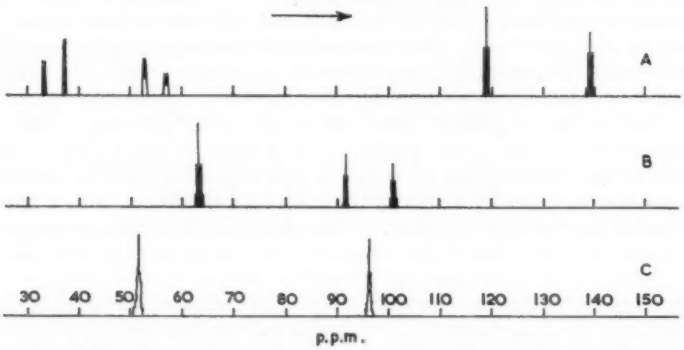
fluorine atoms. The low-field bands arise from the aliphatic fluorine atoms; in the parent compound, as expected, these are all equivalent, producing a band of intensity 4. In the iron compound, however, the presence of two chemically shifted bands in this region shows that two of the aliphatic fluorine atoms are different from the other two; the large doublet splitting of *ca.* 250 c./sec. between them shows that it is the two fluorine atoms of each CF_2 group which are not equivalent, *i.e.*, we have CFF′, probably because one of them is necessarily closer to the metal atom in the $Fe(CO)_3$ group. Since the splitting between the fluorine atoms of the CF_2 group is of the same order of magnitude as the chemical shift between them, their spectrum has the symmetrical appearance of an "AB" pair. A similar difference between two fluorine atoms in a cyclic CF_2 group

^{19}F *magnetic resonance spectra at 56·45 Mc./sec. (external reference, benzotrifluoride); fields increase to the right.*



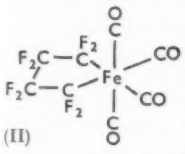
A, *Complex* $C_8F_8Fe(CO)_3$. B, *Perfluorocyclohexa-1,3-diene*. C, *Perfluorocyclohexa-1,4-diene*.

when one of the atoms is closer to another atom is found in the monosubstituted tetrafluorocyclobutanes,[5] and in the case of protons we have observed several cases of a similar nature [6] when one of the atoms is closer to a metal atom than the other.

The small additional doublet splitting on the aliphatic fluorine lines probably results from the coupling between these atoms and the terminal olefinic fluorine atoms. This splitting is different for the two fluorines in each CFF′ group, suggesting that the C–F bonds make different angles with the $\diagdown C=$ bond.
$\quad\quad\quad

carbon–carbon distances in co-ordinated conjugated olefins are the same, and we cannot be certain on this point with the evidence to hand. Certainly, however, proton resonances are more susceptible both to small electron-density effects and also to long-range shielding effects of π-electron systems than are fluorine resonances, so that the large separations observed are not necessarily inconsistent with the view that the carbon–carbon distances are the same in the co-ordinated conjugated diene system.

Perfluorotetramethyleneiron Tetracarbonyl.—The reaction of tetrafluoroethylene with tri-iron dodecacarbonyl leads to a colourless crystalline compound of properties very similar to the diene derivative noted above. On the basis of analytical data which are now known to have been unreliable, mainly owing to difficulties in removing traces of impurities by sublimation with the small quantities of the material originally available, this compound was first believed to be the tricarbonyl. Mass-spectroscopic measurements unequivocally showed that the compound is a tetracarbonyl, as did the *X*-ray molecular-weight determination. Further, a comparison of the fluorine resonance integrated peak areas for known weights of the compound and benzotrifluoride in acetone gave a molecular weight of 373. Thus the stoicheiometry and the spectroscopic studies are consistent with the structure (II) in which a $[-CF_2-]_4$ chain is bound to the iron atom by σ-bonds. The nuclear magnetic resonance spectrum shows two lines of equal intensity (2 : 2) in the region of other aliphatic C–F bonds. Both lines appear to be approximately triplets with a splitting of *ca.* 2·5 c./sec., which is consistent with the spin-coupling between non-equivalent aliphatic CF_2 groups.


(II)

Mass spectra of $C_6F_8Fe(CO)_3$ *and* $C_4F_8Fe(CO)_4$.—A partial mass spectrum of the key ion fragments, detected when $C_4F_8Fe(CO)_4$ was sublimed into a mass spectrometer at 25°, is shown in Table 1.

TABLE 1. *Partial mass spectrum of* $C_4F_8Fe(CO)_4$.

Mass no.	Fragment ion	Peak intensity *	Mass no.	Fragment ion	Peak intensity *
368	$C_4F_8Fe(CO)_4^+$	2·3	284	$C_4F_8Fe(CO)^+$	9·1
340	$C_4F_8Fe(CO)_3^+$	34·1	256	$C_4F_8Fe^+$	2·0
312	$C_4F_8Fe(CO)_2^+$	17·1	162	$C_4F_6^+$	100·0

* Relative to $C_4F_6^+$ ion peak as 100.

The fragment ion of mass 368 is an important one in that it determines the molecular weight of the compound. This result is of special interest because many of the conventional methods for determination of molecular weight give unreliable values for the iron carbonyl derivative. The detection of an ion assignable to $C_4F_8Fe(CO)_4$ is unique since metal carbonyl compounds often lose carbon monoxide so easily that the ion required for the molecular weight is not seen in the mass spectrum.

The ions of mass 340, 312, 284, and 256 corresponding to $C_4F_8Fe(CO)_3^+$, $C_4F_8Fe(CO)_2^+$, $C_4F_8Fe(CO)^+$, and $C_4F_8Fe^+$, respectively, are formed by a stepwise loss of carbon monoxide from the parent compound. One might expect the $C_4F_8Fe^+$ ion to break up stepwise also, to give $C_4F_8^+$ and $C_4F_7^+$ ions, but these fragments do not appear in the mass spectrum. The largest iron-free fragment in the spectrum is the $C_4F_6^+$ ion. This fragment of mass 162 is one of the major ions in the spectrum, and its abundance appears to be related to the ease with which $C_4F_8Fe(CO)_4$ decomposes to give perfluorocyclobutene when heated. It was found, for example, that introduction of $C_4F_8Fe(CO)_4$ into the mass spectrometer through an inlet maintained at 150° gives the mass spectrum of perfluorocyclobutene and no ions of mass larger than 162.

A partial mass spectrum of the ion fragments observed when $C_6F_8Fe(CO)_3$ was sublimed into a mass spectrometer is shown in Table 2.

The mass spectrum of $C_6F_8Fe(CO)_3$ is similar to that of $C_4F_8Fe(CO)_4$ in the appearance of the ions $C_6F_8Fe(CO)_3^+$, $C_6F_8(CO)_2^+$, $C_6F_8Fe(CO)^+$, and $C_6F_8Fe^+$ that correspond to the

TABLE 2. *Partial mass spectrum of* $C_6F_8Fe(CO)_3$.

Mass no.	Fragment ion	Peak intensity *	Mass no.	Fragment ion	Peak intensity *
364	$C_6F_8Fe(CO)_3^+$	4·0	224	$C_6F_8^+$	1·1
336	$C_6F_8Fe(CO)_2^+$	4·0	205	$C_6F_7^+$	2·5
308	$C_6F_8Fe(CO)^+$	0·1	186	$C_6F_6^+$	100·0
280	$C_6F_8Fe^+$	0·36			

* Relative to $C_6F_6^+$ ion peak at 100.

parent compound and the fragments formed by successive loss of carbon monoxide. Formation of $C_6F_6^+$ as the major fluorocarbon ion is also similar to that of $C_4F_6^+$ from $C_4F_8Fe(CO)_4$. It should be noted, however, that $C_6F_8Fe(CO)_3$ shows important differences from $C_4F_8Fe(CO)_4$ in fragmentation behaviour. For example, the fragments $C_6F_8Fe(CO)_2^+$, $C_6F_8Fe(CO)^+$, and $C_6F_8Fe^+$ are not as abundant in the mass spectrum of $C_6F_8Fe(CO)_3$ as the corresponding ions derived from $C_4F_8Fe(CO)_4$. Another significant feature of the behaviour of $C_6F_8Fe(CO)_3$ is the formation of the ions $C_6F_8^+$ and $C_6F_7^+$ as well as $C_6F_6^+$. There is also a sharp contrast between these two iron compounds with regard to the ease with which $Fe(CO)_x^+$ fragments are formed. The partial mass spectrum shown in Table 3

TABLE 3. *Partial mass spectrum of* $C_6F_8Fe(CO)_3$ *and* $C_4F_8Fe(CO)_4$.

Mass no.	Fragment ion	Peak intensity relative to $C_6F_6^+$ from $C_6F_8Fe(CO)_3$	Peak intensity relative to $C_4F_6^+$ from $C_4F_8Fe(CO)_4$	Mass no.	Fragment ion	Peak intensity relative to $C_6F_6^+$ from $C_6F_8Fe(CO)_3$	Peak intensity relative to $C_4F_6^+$ from $C_4F_8Fe(CO)_4$
168	$Fe(CO)_4^+$	—	0·4	84	$Fe(CO)^+$	103·2	61·9
140	$Fe(CO)_3^+$	49·1	2·2	56	Fe^+	79·9	56·5
112	$Fe(CO)_2^+$	192·1	60·5	28	CO^+	10·6	185·6

shows that $Fe(CO)_2^+$ and $Fe(CO)^+$ are the major ions in the fragmentation of $C_6F_8Fe(CO)_3$. The situation with regard to the abundance of CO^+ ion in the two spectra is just the reverse. These differences in fragmentation behaviour of $C_6F_8Fe(CO)_3$ and $C_4F_8Fe(CO)_4$ indicate a fundamental difference in the bonding of the iron to the fluorocarbon part of the molecule, in accord with the other evidence presented above.

Other Derivatives.—Reaction of tetrafluoroethylene with cobalt carbonyl gives a compound $(CO)_4Co[CF_2]_2Co(CO)_4$ which is like the iron compound in being a normal σ-bonded derivative. With di-π-cyclopentadienylcobalt a binuclear species is also obtained but here the $-[CF_2]_2-$ group bridges the *endo*-positions of two π-cyclopentadienylcobalt cyclopentadiene units; this structure is confirmed by results of nuclear resonance measurement, and a comparison can readily be made with similar cyclopentadiene compounds [6] and particularly with the compound π-$C_3H_5CoC_5H_5$·CF_3 resulting from the interaction of trifluoromethyl iodide and $(\pi$-$C_5H_5)_2Co$. For the latter, the fluorine resonance [6] is a doublet split by the H_β proton, and conversely the H_β proton resonance line (triplet) is further split into a quadruplet by the three fluorine nuclei. In $[\pi$-$C_5H_5CoC_5H_5$·$CF_2-]_2$, the fluorine resonance is again a doublet split by H_β and occurs in the normal aliphatic C–F region; the proton spectrum shows a single line from the π-C_5H_5 protons, a " triplet " band from the central diene protons, and a band at higher field from the terminal diene protons. The remaining band is assigned to the H_β proton, and it would have been expected that it would show splitting by both CF_2 groups and that the terminal diene protons would give a triple triplet, but it was not possible to resolve this structure.

EXPERIMENTAL

Microanalyses and molecular-weight measurements (ebullioscopic in benzene) were made by the Microanalytical Laboratory, Imperial College, and, together with mass-spectrometric analyses, also by the Physical and Analytical Division, Central Research Department, Experimental Station, E. I. du Pont de Nemours and Co.

Octafluorocyclohexa-1,3-dieneiron Tricarbonyl.—In a typical preparation $Fe_3(CO)_{12}$ (2 g.) was sealed with octafluorocyclohexa-1,3- or -1,4-diene (*ca.* 3 g.) in a thick-walled glass tube. During

the heating at 120—130° for *ca.* 12 hr., the contents of the tube became dark brown. After cooling in liquid oxygen, the tube was opened and the excess of olefin and other volatile products removed. Extraction of the solid residue with light petroleum (b. p. 40—60°) gave a yellow-orange solution from which at −80° pale yellow crystals separated. The *product* was purified by recrystallisation and sublimation in a vacuum from *ca.* 30° to a probe at −80° [yield, *ca.* 1·38 g., *ca.* 31% based on $Fe_3(CO)_{12}$; m. p. 45°] [Found: C, 29·6, 28·5, 28·2; F, 40·7, 41·2; Fe, 15·0, 15·9. $C_6F_8Fe(CO)_3$ requires C, 29·7; F, 41·8; Fe, 15·3%]. Solutions in organic solvents undergo extensive decomposition in a few hours, even in the absence of air; ebullioscopic molecular-weight determinations gave values *ca.* 500, presumably owing to loss by volatilisation or decomposition.

The density was determined by the standard flotation method in aqueous barium mercuric iodide solutions and a value of 2·133 ± 0·007 g./c.c. was obtained; *X*-ray diffraction studies gave the dimensions of the orthorhombic unit cell as $a = 13{\cdot}38$, $b = 6{\cdot}85$, $c = 11{\cdot}88$ Å; the molecular weight is 361, the space group being $Pca2_1$.

Octafluorotetramethyleneiron Tetracarbonyl.—Tetrafluoroethylene was prepared by cracking polytetrafluoroethylene (I.C.I. powder) at *ca.* 500°. The gas was condensed and then taken off from a trap at −80° through soda-lime before use. About 3 g. of tetrafluoroethylene were condensed on to *ca.* 2 g. of $Fe_3(CO)_{12}$ in a thick-walled glass tube. After the sealed tube had been heated at 110—120° for 10—15 hr. it was cooled in liquid oxygen and opened and the excess of olefin and volatile material [mainly $Fe(CO)_5$] were removed. The residue was dissolved and the product crystallised from light petroleum (b. p. 40—60°) at −80° and finally sublimed in a vacuum from 40° to a probe at −80° (yield, *ca.* 100 mg.; m. p. 77—78°). On a larger scale the compound is best extracted from the residues with ethyl acetate (in which it is very soluble); the solution is filtered, methylcyclohexane is added, and the ethyl acetate (which distils first) is removed in a vacuum, whereupon the *product* separates as snow-white crystals [Found: C, 26·5, 26·5; F, 41·7; Fe, 15·4. $C_4F_8Fe(CO)_4$ requires C, 26·1; F, 41·3; Fe, 15·2%]. The density by flotation in aqueous solutions of barium mercuric iodide was 2·097 ± 0·001 g./c.c. and *X*-ray diffraction showed a monoclinic cell, with $a = 12{\cdot}86$, $b = 7{\cdot}55$, $c = 13{\cdot}58$ Å, $\beta = 116{\cdot}4°$, leading to a molecular weight of 373. The compound decomposes within a few hours in organic solvents; it is stable to dilute acids but is decomposed by sodium hydroxide. From molten $C_4F_8Fe(CO)_4$ gas evolution begins at 150° and is rapid at 185°; this is consistent with the pyrolysis of the compound to perfluorocyclobutane, mentioned in connection with the mass-spectrometric studies.

Octacarbonyl-μ-tetrafluorodimethylenedicobalt.—Cobalt carbonyl (1 g.) was sealed with an excess of tetrafluoroethylene and held at 25° for 10 days. After removal of the excess of olefin and carbonyl at 60° in a vacuum the residue crystallised from light petroleum (b. p. 30—40°) at −80°. Sublimation in a vacuum gave the *compound* as orange crystals [*ca.* 30%, based on $Co_2(CO)_8$], m. p. 80° (decomp.) (Found: C, 27·0; F, 16·4; Co, 26·2. $C_{10}F_4Co_2O_8$ requires C, 27·2; F, 17·2; Co, 26·7%). The compound is moderately stable in air but decomposes in solution in organic solvents (in which it is quite soluble), quite rapidly in air though in absence of air the solutions are stable for some hours; the compound decomposes in boiling benzene in absence of air.

Di-(π-cyclopentadienylcobalt)-endo-μ-tetrafluorodimethylenecyclopentadiene.—Di-π-cyclopentadienylcobalt (2 g.) in tetrahydrofuran (10 ml.) was sealed with tetrafluoroethylene (10 ml.; liquid) for 2 days at 25°. The volatile materials were removed and the residue was extracted (Soxhlet) with light petroleum (b. p. 30—80°); cooling to −80° gave a crystalline red-brown *product* (0·5 g.), decomp. 140° without melting (Found: C, 55·2; H, 4·4; F, 16·3; Co, 25·7%; *M*, 500. $C_{22}H_{20}Co_2F_4$ requires C, 55·25; H, 4·2; F, 15·9; Co, 24;65%; *M*, 478·3). The compound is sparingly soluble in light petroleum but is moderately soluble in carbon tetrachloride, chloroform, carbon disulphide, and acetone. It is stable in air and moderately so (several hours) in solution.

π-Cyclopentadienyl(endotrifluoromethylcyclopentadiene)cobalt.—$(\pi\text{-}C_5H_5)_2Co$ (0·7 g.) and trifluoromethyl iodide (2 ml.; liquid) were sealed and left at 25°. After 4 days the excess of iodide was removed and the residue extracted with light petroleum (b. p. 40—60°). The blood-red solution was evaporated in a stream of nitrogen and the residual oil distilled to a probe at −80°, giving blood-red crystals [*ca.* 40% based on $(\pi\text{-}C_5H_5)_2Co$] of *complex*, m. p. −10° (Found: C, 50·1; H, 3·8; Co, 23·2. $C_{11}H_{10}CoF_3$ requires C, 51·1; H, 4·0; Co, 22·8%). The compound decomposes above 110° and is readily oxidised in air in the pure state and

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even more rapidly in solution in organic solvents. It is stable in hydrocarbon and other solvents in absence of air.

Infrared Spectra.—Spectra were taken on a Perkin–Elmer model 21 instrument with sodium chloride, calcium fluoride, and potassium iodide prisms in the appropriate regions.

Octafluorocyclohexa-1,3-diene (5 mm. Hg; 10-cm. gas cell): 1750m, 1710m (C=C str.), 1400s, 1352s, 1278m, 1223w, 1176w, 1152s, 1105s, 1020w, 988s, 945m cm.$^{-1}$.

Octafluorocyclohexa-1,4-diene (as above): 2195w, 1785w, 1741s (C=C str.), 1410w, 1375w, 1330s, 1282w, 1242s, 1204w, 1176w, 1150m, 1100s, 1025s, 975s cm.$^{-1}$. The spectra of these olefins in the C=C region only have been reported previously,[9] the values quoted being 1713, 1753 (1,3-), and 1739 (1,4-) cm.$^{-1}$.

$C_6F_8Fe(CO)_3$ (CCl_4, CS_2, and C_2Cl_4 mulls): 2480w; 2108s, 2054vs, 2018m (C–O str.); 1550s (C=C str.); 1455m, 1407m, 1278vs, 1138s, 1105m, 1068m, 1047s, 974s, 941vs, 805w, 723s cm.$^{-1}$.

$C_4F_8Fe(CO)_4$ (CCl_4, CS_2, and C_2Cl_4 mulls): 2480w; 2160s, 2108vs, 2088vs, 2055s (C–O str.); 1332m, 263m, 1228m, 1170s, 1103s, 1060s, 968s, 910s, 720m, 647s, 628w, 610w, 575s, 520m, 492m, 437m cm.$^{-1}$.

$(CO)_4Co(CF_2)_2Co(CO)_4$ (CCl_4 and CS_2): 2480w, 2430w; 2130s, 2070vs, 2025vs, 1940m (C–O) str.); 1218s, 1048m, 925w, 785s, 767vs, 675s cm.$^{-1}$.

(π-$C_5H_5CoC_5H_5$-*endo*-CF_2–)$_2$ (CCl_4, CS_2 and C_2Cl_4 mull): 3090m (C–H str. of π-C_5H_5), 2940w (C–H$_\beta$ str.), 1420w, 1383w, 1346w, 1336w, 1322m, 1250w, 1220m, 1146s, 1108m, 1088s, 1070m, 1050m, 1007m, 998m, 962m, 912w, 908w, 875w, 853w, 836m, 805s, 692s, 655m cm.$^{-1}$.

π-$C_5H_5CoC_5H_5CF_2$ (CCl_4): 3070w (C–H str. of π-C_5H_5), 2930w (C–H$_\beta$ str.), 1835m, 1785m, 1340m, 1255m, 1230m, 1203m, 1183m, 1142s, 1127s, 1077m, 1033m, 938m, 675m cm.$^{-1}$.

Mass-spectrometric Analysis.—A Consolidated 21-103C mass spectrometer was used to record the mass spectra of $C_4F_8Fe(CO)_4$ and $C_6F_8Fe(CO)_3$. The conditions employed for $C_4F_8Fe(CO)_4$ were as follows: inlet temperature 25°, source temperature 250°, and current 10·5 microamp. The following conditions were used for obtaining the mass spectrum of $C_6F_8Fe(CO)_3$: inlet temperature 25°, source temperature 250°, current 15 and 60 microamp. The sample holder was heated at 55° in the analysis of $C_6F_8Fe(CO)_3$, but no heating of the sample was required for $C_4F_8Fe(CO)_4$.

High-resolution Nuclear Magnetic Resonance Spectra.—The spectra were recorded with Varian spectrometers V-4311 and 4310C at frequencies of 56·45 and 40 Mc./sec. The samples were contained in 5-mm. (outside diameter) Pyrex spinning tubes. Line positions were measured by the conventional side-band technique. Tetramethylsilane was added to the solutions as an internal reference for protons, and shifts are given in τ-values. Fluorine resonance line positions are given in p.p.m. relative to benzotrifluoride, positive values representing lines on the high-field side of this reference.

Perfluorocyclohexa-1,3-diene (liquid, reference external): 63·20, approx. triplet (13·2 $\pm$ 1 c./sec.) with additional structure, including weak components at $\pm$31 c./sec. from centre, CF_2 groups, split by F_1 and F_4; 91·55, " triplet " (15·2 $\pm$ 1 c./sec.), F_2 and F_3, each split by F_1 and F_4; 100·9$_5$, approx. pentuplet (inner components 13·4 c./sec., outer components 30·6 c./sec., from centre) with finer structure (? quartets) ~1·5 c./sec., F_1 and F_4, split by F_2 and F_3, and by nearest CF_2 group.

Perfluorocyclohexa-1,4-diene (liquid, reference external): 51·43, complex multiplet, CF_2 groups; 96·30, complex multiplet, =CF groups.

$C_6F_8Fe(CO)_3$ (in CCl_4 solution, reference external): (*a*) 35·4; centre (calculated for "A" of an "AB" pair) of each of two equivalent ^{19}F nuclei, one in each CF_2 group, split into an unsymmetrical doublet (232·1 $\pm$ 1 c./sec.) by the non-equivalent " B " fluorine nucleus in the same CF_2 group, and again into a doublet (18·2 $\pm$ 0·7 c./sec.) by the adjacent fluorine nucleus F_1 or F_4. Each of the resulting four component lines has additional unresolved fine structure ($\frac{1}{2}$ width of lines ~7 c./sec.).

(*b*) 54·70, centre (calculated for " B " of "AB" pair) of each of two equivalent ^{19}F nuclei, the others in each CF_2 group, doublet (232 $\pm$ 1 c./sec.) doublet (14·2 $\pm$ 1 c./sec.), latter by coupling with adjacent F_1 or F_4. Additional unresolved coupling (not identical with that of "A" nuclei) gives $\frac{1}{2}$ width of about 15 c./sec.

(*c*) 119·4, approx. triple (19·4 $\pm$ 1 c./sec.) triplet (3·4 c./sec.), $F_2 + F_3$ split by F_1 and F_4, and by the nearest CF_2 group (3·4 c./sec.).

[9] Evans and Tatlow, *J.*, 1954, 3779.

(*d*) 139·5, approx. pentuplet (18·2 ± 1 c./sec.) with additional (? quartet) structure (~3—4 c./sec.), $F_1 + F_4$, split by F_2 and F_3 and by the adjacent CF_2 group.

$C_4F_8Fe(CO)_4$ (in CCl_4, internal reference): 9·25, approx. pentuplet (1 : 4 : 5 : 4 : 1), (~2·5 c./sec.), central CF_2 groups; 73·95, approx. pentuplet (1 : 5 : 10 : 5 : 1), (~2·6 c./sec.), terminal CF_2 groups.

$[(CO)_4CoCF_2-]_2$ (in CCl_4, internal reference): −30·7, single fluorine resonance line, width ⩽2 c./sec.

$[\pi\text{-}C_5H_5CoC_5H_5CF_2-]_2$ (in CCl_4, external reference): fluorine resonance: 62·2, doublet (13·5 c./sec.), split by methylene proton H_β. Proton resonance: 5·08, " triplet " (2 c./sec.), $H_3 + H_4$ split by $H_2 + H_5$; 4·62, singlet, $\pi\text{-}C_5H_5$ group; ~3·1 (very weak), H_β; 2·37, $H_2 + H_5$.

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Inorganic Chemistry Research Laboratories,
Imperial College of Science and Technology,
S. Kensington, London, S.W.7.
(H. H.) Central Research Department, Experimental Station,
E.I. du Pont de Nemours and Co.,
Wilmington, Del.

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536. *Effect of Defect Structure on the Rate of Formation of Spinels.**

By F. Solymosi and Z. G. Szabó.

The effect of electronic and ionic-defect structure on the rate of formation of nickel ferrite spinel was investigated; the reaction was followed by magnetic analysis. Nickel oxide was doped with small amounts of lithium and chromic oxides, and ferric oxide with titanium dioxide. The addition of foreign ions markedly influences the rate of formation of the spinel, especially in the case of nickel oxide doped with chromic oxide. The variation of electrical resistance of these mixed oxides during formation of spinel was also studied.

The rate of reaction between two solid phases is governed by migration of the reactants, which in turn depends on the structure of the reacting crystals or crystallites. Features such as lattice defects and vacant sites promote the migration and thus increase the reaction rate. In this respect the Hedvall effect is an extreme case as the disorder is greatest during lattice transition.

The defect structure in crystals can be changed to a large extent by pretreatment or by doping with foreign ions. Thus it may be expected that the rate of reaction between two solids depends on doping as well as on the morphology of the initial substances. The influence of foreign ions on this rate permits them to be considered as catalysts, since they remain more or less unchanged at the end of the process.

Solid-phase reactions play a major part in the preparation of contact catalysts, consisting of mixtures of oxides, in which the first of several processes occurring is the formation of spinels. We have postulated, on the basis of electrical conductivity measurements, the nature of the catalytic activity and origin of the intermediate states formed during spinel formation.[1] The optimum catalytic activity was to be attributed to a certain state

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[1] Szabó and Solymosi, *Z. Elektrochem.*, 1959, **63**, 1177.

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of the solid system, determined by exactly described parameters. The permanence of this optimum state depends both on the conditions of formation and the mechanism of further reaction. The best contact substance is obtained when the optimum catalysing system has been formed under conditions in which the further reaction is negligibly small.

In our experiments the problem of rates of reaction in solid phases has been investigated with mixed oxides of varied composition (*i.e.* with known " Fehlordnung "), with special emphasis on spinel formation. The only analogous investigations are those of Schwab and Rau.[2] The rates of solid-phase reactions are generally difficult to determine. In our experiments the formation of nickel ferrite from nickel oxide and ferric oxide was chosen, since the reaction can be followed by measurement of the magnetic susceptibility, because of the strong ferromagnetic properties of the nickel ferrite formed. The magnetic properties of this spinel and the effect of different gases on the reaction rate have been investigated by Forestier and his co-workers.[3] Electrical conductivity gives a qualitative picture of the possible intermediate states formed during the reaction, so it has also been investigated as a function of the sintering temperature.

Experimental

The nickel oxide was pretreated by heating it in air for 5 hr. at 1000—1050°, and the standardized properties were controlled by electrical-conductivity measurements. Pellets

Fig. 1. *Resistance of mixed oxides at 250°, and the activation energy of conductivity as a function of the reaction temperature.*

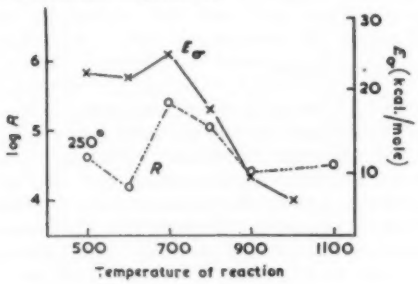
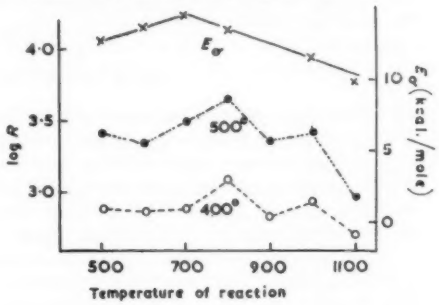


Fig. 2. *Resistance of mixed oxides at 400° and 500°, and the activation energy of conductivity as a function of the reaction temperature.*



were prepared from nickel and ferric oxides in the proportion 1 : 1, and were sintered for 5 hr. at different temperatures. The sintered product was cooled quickly in order to freeze-in the intermediate states formed. The electrical conductivity of these pellets was then examined at different temperatures. At temperatures below 300° the conductivity soon reached a steady value, while at higher temperatures a longer time was required, but this value was reproducible and remained unchanged by further heating. From these data a value of E, the activation energy of electrical conductivity, was obtained. Figs. 1 and 2 illustrate these results. Both the resistance and activation energies show maxima at a sintering temperature of 700° for lower-temperature, and at a sintering temperature of 800° for higher-temperature measurements.

Magnetic susceptibility and X-ray diffraction investigations were performed to interpret this behaviour. The magnetic susceptibility measurements were made by Gouy's method and the values at two different field strengths are shown in Fig. 3. These values indicate that spinel formation begins at 650—700°, whereas the less sensitive method by X-ray powder photograph first detected nickel ferrite lines at 750°. From these measurements we can state that at the beginning of spinel formation an intermediate state with special properties appears.

The nature of this intermediate state was clarified by experiments carried out at different

[2] Schwab and Rau, *Z. phys. Chem.* (*Frankfurt*), 1956, **9**, 127; 1958, **17**, 257.
[3] Forestier and Kiehl, *J. Chim. phys.*, 1950, **47**, 165; *Compt. rend.*, 1949, **229**, 47; Forestier and Haasser, *Compt. rend.*, 1947, **225**, 188.

partial pressures of oxygen. Before spinel formation, the conductivity of the mixed oxides increases with the partial pressure of oxygen, while after spinel formation the conductivity changes inversely with the partial pressure of oxygen. However, at 700° the conductivity changes from the defect conductivity of mixed oxides to the electron conductivity of spinels, with the resulting maxima of resistance and activation energy already noted.

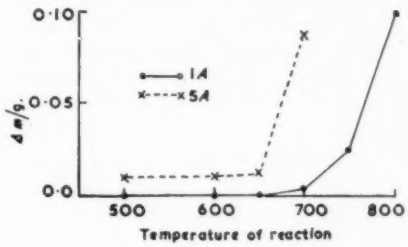


FIG. 3. *Changes in magnetic susceptibility expressed as the increase of weight related to* 1 *g. of substance as a function of reaction temperature. Time of reaction*: 5 *hr.*

The rate of reaction of the solid phase can be estimated from the changes in magnetic susceptibility. One hour's sintering produced a change of only −0·05—1·0%; thus only a surface reaction has occurred.

In addition to these pure oxide mixtures, doped oxides have been investigated. The conductivity was increased by addition of lithium oxide to nickel oxide, but decreased by addition of chromium(III) oxide, in accordance with the *p*-conducting character of nickel oxide. The doped oxides were sintered separately for 5 hr. at 850—900°, mixed in equal proportions in a ball mill for several hours and then heated for 1 hr. After the reaction the mixture was powdered in an agate mortar and the susceptibility determined in a glass tube (3 mm. diam.).

The data obtained are shown in Fig. 4 and are averages of four readings, obtained by use of two sensitivities together with a reversal of current.

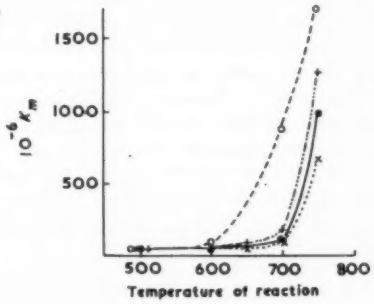


FIG. 4. *Changes in magnetic susceptibility at* 5A *as a function of temperature. Time of reaction*: 1 *hr.*

——— $NiO–Fe_2O_3$.
····· $NiO–Fe_2O_3 + 1\%\ TiO_2$.
– – – – – $NiO + 1\%\ Cr_2O_3–Fe_2O_3$.
·—·—· $NiO + 1\%\ Li_2O–Fe_2O_3$.

Mixtures containing nickel oxide doped with lithium and chromic oxides show a considerable increase in susceptibility over pure mixed oxide mixtures, even after 1 hr. On the other hand, addition of titanium dioxide to ferric oxide reduces the susceptibility. Thus doping by chromic oxide represents a catalysed reaction, and by titanium dioxide an inhibited reaction.

Fig. 5 shows the rate data in detail, but the ordinate plotted here is the weight increase related to 1 g. of the mixture.

The increase in the weight of the mixture can be considered as the reaction rate. Satisfactory linear functions can be obtained by plotting the logarithms of these values against $1/T$ between 700° and 800°.

From these relations the following apparent activation energies have been calculated:

$NiO–Fe_2O_3$, 95·9; $NiO + 1\%Li_2O–Fe_2O_3$, 80·0;
$NiO + 1\%Cr_2O_3–Fe_2O_3$, 59·4; and $NiO–Fe_2O_3 + 1\%TiO_2$, 132·3 kcal./mole.

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These values are in good agreement with those of Schwab and Rau [3] (58—82 kcal./mole) and of Hopkins [4] (57, 102 kcal./mole) for the reaction of zinc oxide and ferric oxide.

FIG. 5. *Changes in magnetic susceptibility at* 1A *expressed as the increase of weight related to* 1 *g. of substance as a function of reaction temperature. Time of reaction*: 1 *hr.*

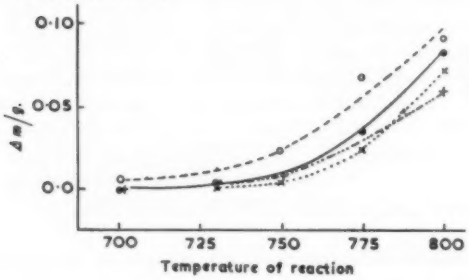
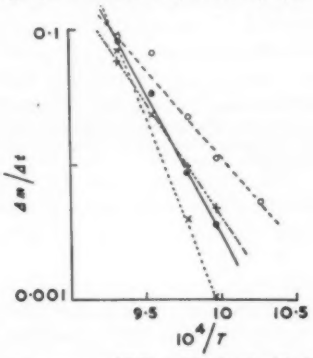


FIG. 6. *Logarithm of weight increase related to* 1 *g. of substance as a function of* 1/T.



——— $NiO–Fe_2O_3$. ····· $NiO–Fe_2O_3 + 1\%\ TiO_2$. – – – – – $NiO + 1\%\ Cr_2O_3–Fe_2O_3$. ···—··· $NiO + 1\%\ Li_2O–Fe_2O_3$.

DISCUSSION

The results obtained can be interpreted in the light of the " Fehlordnung " theory. The decrease in the rate of reaction on doping ferric oxide with titanium dioxide is probably due to the formation of ferrous ions. Verwey and his associates [5] have concluded, from conductivity measurements, that iron(II) ions are formed and that the larger diameter of these ions reduces their mobility and consequently their rate of diffusion.

According to Wagner and Hauffe's theory the product of the concentrations of the vacant nickel sites and the defect electrons is constant under a constant pressure of oxygen. This explains the effect of chromium(III) oxide on nickel oxide, when the conductivity decreases, *i.e.*, the concentration of defect electrons decreases and so the number of vacant sites increases. Thus, both the diffusion and consequent rate of reaction are increased.

Doping with lithium oxide results in the formation of Ni^{3+} ions in the nickel oxide lattice, and the greater mobility of these increases the reaction rate.[2]

Summarizing, we can say that in the nickel oxide–ferric oxide system, the rate of spinel formation depends on the defect structure of the initial substances. When the defect structure of these is altered by doping a catalytic or inhibiting effect on the reaction rate is observed.

UNIVERSITY OF SZEGED, INSTITUTE FOR INORGANIC AND ANALYTICAL CHEMISTRY,
SZEGED, HUNGARY. [*Received, May* 13*th*, 1960.]

[4] Hopkins, *J. Electrochem. Soc.*, 1949, **96**, 195.
[5] Verwey, Haayman, and Romeyn, *Chem. Weekblad*, 1948, **44**, 705.

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537. *The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part X.*[1] *Products in the Chlorination of Biphenyl in Acetic Acid.*

By G. H. Beaven, P. B. D. de la Mare, M. Hassan, E. A. Johnson, and N. V. Klassen.

The products of reaction of biphenyl with chlorine in acetic acid have been examined, particularly by vapour-phase chromatography and isotopic dilution analysis. The $\frac{1}{2}o : p$ ratio is 0·3; very little, if any, 3-chlorobiphenyl is produced; and accompanying the substitution is an addition which consumes *ca.* 14% of the chlorine.

The phenyl group is inductively electron-withdrawing, but can also, when appropriately oriented, withdraw or release electrons conjugatively ($-I$, $\pm T$). Its response to the electronic requirements of a reaction-centre depends on the nature of the reaction, and hence it is sometimes said to have several σ-values, some of different sign.[2] Conjugative effects of substituents can, in principle, be transmitted through one ring of a biphenyl system to the adjoining ring,[3] but the quantitative importance of this effect is variable [4,5] and has not been examined very systematically.

Theoretical calculations [6] which relate reactivities of biphenyl with those of polycyclic aromatic hydrocarbons involve assumptions concerning the magnitude of the energy barrier restricting rotation about the Ar–Ar bond in biphenyl. Current opinions [7] concerning this quantity include values in the range 0—4 kcal. mole^{-1}, and a considerable effect on reaction velocity and on orientation is to be expected from steric inhibition of conjugation in 2-substituted biaryls.[8]

The rate of molecular chlorination in acetic acid depends much on structural effects, and particularly on conjugation.[9] It seemed useful, therefore, to extend our studies to biphenyl and its derivatives. This paper reports the commencement of such an investigation, including a side-reaction of addition (previously not generally recognised for such compounds in this solvent) whose importance is assessed; the more general considerations will be discussed in other papers.

Experimental

Materials and Methods.—Some of the materials and methods have been described in previous papers in this series. 2-Chlorobiphenyl, m. p. 33·5° (lit.,[10] 34°) was prepared from 2-aminobiphenyl by the Sandmeyer procedure. The following compounds were prepared from benzene and commercial specimens of the appropriate amines, by the Gomberg reaction: [11] 4-chlorobiphenyl, m. p. 77°; 3-chlorobiphenyl, b. p. 106—108°/*ca.* 0·1 mm., n_D^{25} 1·6175; 2,4-dichlorobiphenyl, n_D^{25} 1·6169 (Found: C, 64·4; H, 3·7; Cl, 31·5. Calc. for $C_{12}H_8Cl_2$: C, 64·6; H, 3·6; Cl, 31·8%); 2,5-dichlorobiphenyl, n_D^{25} 1·6154 (Found: C, 64·4; H, 3·7; Cl, 31·5%); 3,4-dichlorobiphenyl, n_D^{25} 1·6340 (Found: C, 64·6; H, 3·7; Cl, 31·5%). 3,5-Dichlorobiphenyl, prepared by dichlorination of 2-aminobiphenyl followed by deamination of the product,[12] had

[1] Part IX, de la Mare, Hilton, and Varma, *J.*, 1960, 4044.
[2] Berliner and Liu, *J. Amer. Chem. Soc.*, 1953, **75**, 2417.
[3] Cf. Berliner and Blommers, *J. Amer. Chem. Soc.*, 1951, **73**, 2479.
[4] de la Mare and Ridd, "Aromatic Substitution—Nitration and Halogenation," Butterworths, London, 1959, pp. 157 ff.
[5] de la Mare and Robertson, *J.*, 1948, 100.
[6] Dewar, *J.*, 1957, 342; R. D. Brown, *J.*, 1959, 2224, 2232.
[7] Adrian, *J. Chem. Phys.*, 1958, **28**, 608; Howlett, *J.*, 1960, 1055; H. C. Brown, "Steric Effects in Conjugated Systems" (ed. Gray), Butterworths, London, 1958, p. 104; Coulson, "Theoretical Organic Chemistry," Kekulé Symposium, Butterworths, London, 1959, p. 57.
[8] de la Mare, Hall, Harris, and Hassan, *Chem. and Ind.*, 1958, 1086.
[9] Ref. 4, pp. 131 ff.
[10] Cf. Elks, Haworth, and Hey, *J.*, 1940, 1284; Augood, Hey, and Williams, *J.*, 1953, **44**.
[11] Cf. Bachmann and Hoffman, "Organic Reactions," Vol. II, Wiley, New York, 1944, p. 224.
[12] Scarborough and Waters, *J.*, 1927, 89.

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n_D^{25} 1·6257 (Found: C, 64·5; H, 3·8; Cl, 31·6%). They were purified by chromatography on silica gel, light petroleum (b. p. 40—60°) being used for elution. Vapour-phase chromatography showed them to be uniform and therefore almost certainly of high purity.

The infrared spectra are recorded in the Table. They were determined with a Grubb–Parsons double-beam spectrophotometer, solids being in Nujol mull, liquids as films between rock-salt plates. In our experience, small amounts (less than 5%) of 3-chlorobiphenyl were difficult to detect in admixture with the other isomers, especially when biphenyl also was present.

4-Chloro-4′-nitrobiphenyl was prepared by treating 4-chlorobiphenyl (4·2 g.) in acetic acid (10 ml.) with nitric acid (*d* 1·5; 4·2 ml.). The mixture was boiled under reflux for 2 hr. and then poured on ice. The solid was passed in benzene through a column of alumina. Elution and removal of the solvent gave a solid which on recrystallisation from ethanol had m. p. 144°, unchanged on further repeated crystallisation (Found: C, 61·6; H, 3·8; Cl, 15·6; N, 5·8. Calc. for $C_{12}H_8ClNO_2$: C, 61·6; H, 3·4; Cl, 15·2; N, 6·0%). Oxidation with chromic oxide in 75% acetic acid gave *p*-nitrobenzoic acid, m. p. and mixed m. p. 241°. The m. p. (144°) which we now record for 4-chloro-4′-nitrobiphenyl accords with that (143°) given by Angeletti,[13] who prepared the compound from 4-amino-4′-nitrobiphenyl by the Sandmeyer procedure; we did not succeed in attaining a m. p. as high as that (157°) given by Le Fèvre and Turner[14] for material obtained by catalysed chlorination of 4-nitrobiphenyl.

The dinitration of 4-chlorobiphenyl does not seem to have been described previously. We heated 4-chlorobiphenyl (4 g.) with sulphuric acid (3 ml.; *d* 1·89) and nitric acid (3 ml.; *d* 1·42) on a steam-bath for 1 hr. The product was poured on ice and washed with water. The organic product was treated with ether. The insoluble 4-chlorodinitrobiphenyl, recrystallised from ethanol, had m. p. 188—189° (Found: C, 51·6; H, 2·7; Cl, 13·1; N, 10·0. $C_{12}H_7ClN_2O_4$ requires C, 51·7; H, 2·5; Cl, 12·7; N, 10·1%). The ether-soluble fraction was also recrystallised from ethanol; it was another 4-chlorodinitrobiphenyl, m. p. 142—143° (Found: C, 51·8; H, 2·6; Cl, 12·6; N, 9·4%). One of these compounds should be 4-chloro-2,4′-dinitrobiphenyl obtained by nitration of the 4-chloro-4′-nitrobiphenyl formed first. Since this, by analogy with the behaviour of the dihalogenobiphenyls,[15] is unlikely to give much of the product of 3-nitration, it seems probable that the other isomer that we isolated is 4-chloro-2,2′- or -3,2′-dinitrobiphenyl, obtained through 4-chloro-2′-nitrobiphenyl; this compound, by analogy with the behaviour of 4,4′-dihalogeno-2-nitrobiphenyls,[15] might give a mixture of 3- and 2-nitro-derivatives.

The infrared spectra are tabulated.

Analyses by Isotopic Dilution.—(a) *4-Chlorobiphenyl.* (i) Biphenyl (0·1637 mole) was allowed to react completely with ^{36}Cl-labelled chlorine (0·0573 mole) in acetic acid at 25° in the dark. To a portion of the mixture was added a known weight of 4-chlorobiphenyl. The diluted products were then isolated, and oxidised with aqueous potassium permanganate. *p*-Chlorobenzoic acid was repeatedly crystallised to constant m. p. (237—238°) and radioactivity. The molar activity, compared with that of the original chlorine (converted into lithium chloride for radioactive counting) gave the result that, of the chlorine undergoing reaction, 46·6 moles % had reacted to give 4-chlorobiphenyl by substitution.

(ii) In a similar experiment in which 0·261 mole of biphenyl had reacted with 0·0312 mole of chlorine, 4-chlorobiphenyl was isolated directly from the diluted mixture; the radioactivity of this indicated that the reaction gives 46·2 moles %. A further sample was nitrated, as described above; the 4-chloro-4′-nitrobiphenyl, m. p. 144°, had a radioactivity unchanged on repeated crystallisation which corresponded with the formation of 46·6 moles % of 4-chlorobiphenyl.

(b) *2-Chlorobiphenyl.* (i) An attempt to determine the percentage of this isomer by oxidising the mixture after dilution with synthetic 2-chlorobiphenyl gave too high a value (53%). We attribute this to the presence of materials other than 2-chlorobiphenyl which are oxidised to *o*-chlorobenzoic acid. The following method gave a more reliable value.

(ii) The organic product was recovered from the diluted mixture and fractionally distilled *in vacuo*; biphenyl was removed at 115—116°/5 mm.; the remainder distilled at 108°/2 mm. The last fraction, crystallised from alcohol, had m. p. 33·5°, and its radioactivity, unchanged

[13] Angeletti, *Giorn. Farm. Chim.*, 1926, **75**, 262; *Chem. Zentr.*, 1926, II, 3045.
[14] Le Fèvre and Turner, *J.*, 1928, 253.
[15] Shaw and Turner, *J.*, 1932, 285; Marler and Turner, *J.*, 1931, 1359; 1937, 266.

Infrared spectra (cm.$^{-1}$; range 650—1600) of some chlorobiphenyls.

Chloro-substituent(s)								
2-	3-	4-	2,4-	2,5-	3,4-	3,5-	2,2'-	4,4'-
679m	683m				683sh	680sh	662m	
696s	694s	693s	695s	695s	693s	692s	695m	699m
721w			714w				719m	
746s							730m	720m
757sh	752s	756s	760s	763s	765s	766s	752s	810s
767m								
	789s		809s	810s	818s	798s		
		829s	818sh					
	879s		865m	880m	879m	852s	855w	846m
913w						871m		
942w						908w	943w	
						970w	978w	998m
1010m	1001m	1008m	1005m	1013m			1000m	
1036s	1020m		1032m	1032s	1024s		1021m	1015m
	1047s		1070m	1073w	1043w	1060m	1029m	
1076s	1082s				1075w	1073w	1052s	
	1099s	1092s	1099s	1098s		1092m	1079m	1082m
1128m				1131m	1129s	1118m	1122m	1096w
							1153w	1163w
	1258w			1241w	1250w	1278m	1235w	
					1285w		1255w	1290w
	1282w		1370m		1370m	1376w	1370s *	1370s *
	1412s	1406w	1439m	1417m	1431sh	1406m	1418s	
	1470sh		1460s	1438m	1456s	1428m	1447s *	1447s *
				1450s		1448w		
	1481s		1543m	1551w	1547w	1492m		
1508w	1571s		1583m	1586w	1587w	1552s	1555w	
	1600s		1600w			1583s		

* Nujol peaks.

on recrystallisation, corresponded to presence of 29·5% of 2-chlorobiphenyl in the product. A rather less pure fraction was nitrated as recommended by Mascarelli and Gatti.[16] There was obtained 2-chloro-4',5-dinitrobiphenyl, m. p. 159—160°, with a radioactivity which corresponded to 29·8% of 2-chlorobiphenyl in the original mixture (Found: C, 52·3; H, 2·9; Cl, 12·7; N, 10·0. Calc. for $C_{12}H_7ClN_2O_4$: C, 51·7; H, 2·5; Cl, 12·7; N, 10·1%). The $\frac{1}{2}o$: p-ratio from these experiments is therefore 0·32.

(c) *3-Chlorobiphenyl.* An attempt was made to estimate this isomer by isotopic dilution. The diluted mixture should have contained 0·66 g. of radioactive chlorobiphenyl together with 10·70 g. of added inactive 3-chlorobiphenyl. The mixture was nitrated with nitric and sulphuric acid; there was obtained a tetranitro-derivative, m. p. 127°, the specific activity of which corresponded to 12·5% of 3-chlorobiphenyl in the product. This value is far too high. It seems probable that exchange of radio-chlorine between the radioactive impurities and the nitrated 3-chlorobiphenyl occurs during the rather drastic conditions of nitration.

(d) *Chlorobenzene.* To an aliquot part of a mixture similar to those described above, chlorobenzene was added. The organic product was recovered and fractionally distilled. The recovered chlorobenzene had negligible radioactivity; on this basis, not more than 0·01% of chlorobenzene could have been formed in the reaction.

Analysis by Vapour-phase Chromatography.—The apparatus was similar to that employed previously,[17] and is described in more detail elsewhere.[18] Quantitative estimates were made on a basis of peak areas, corrected for molecular-weight difference where necessary. Apiezon L or M was used as a stationary phase at 197° for most of the work, but checks of minor components were carried out with other, more polar, stationary phases; in particular, the absence of a significant amount of 3-chlorobiphenyl was confirmed by using a nitrated 2-dodecylnaphthalene as stationary phase, on which the 3- and the 4-isomer are better separated.

With biphenyl in 10-fold excess over chlorine, the ratio 4-chlorobiphenyl : 2-chlorobiphenyl

[16] Mascarelli and Gatti, *Gazzetta*, 1933, **63**, 654; cf. Case, *J. Amer. Chem. Soc.*, 1943, **65**, 2137.

[17] (*a*) Beaven, James, and Johnson, *Nature*, 1957, **179**, 490; (*b*) Johnson, "Steric Effects in Conjugated Systems" (ed. Gray), Butterworths, London, 1958, p. 174.

[18] Johnson, Childs, and Beaven, *J. Chromatog.*, 1960, **4**, 429.

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in the product was 62 : 38 ($\frac{1}{2}o : p = 0{\cdot}31$). Only traces of other materials were detected. Similar results were obtained when a smaller excess of biphenyl was used. Biphenyl (0·19 mole) was allowed to react with chlorine (0·38 mole). The reaction was stopped when 0·08 mole of chlorine remained; the major products and their relative proportions were then as follows: 2-chlorobiphenyl (20 parts); 4-chlorobiphenyl (19 parts); 2,4′-dichlorobiphenyl (5 parts); * and 4,4′-dichlorobiphenyl (9 parts). On Apiezon M at 197° the retention volumes of the monochlorobiphenyls, relative to biphenyl, were: 2-, 1·50; 3-, 2·30; 4-, 2·40. Those of the dichlorobiphenyls are as follows:

Dichlorobiphenyl	2,2′	4,4′	2,4′	2,4	2,5	3,4	3,5
Retention volume	2·25	5·80	3·65	3·25	3·15	5·50	4·70

These agree well with estimated values.[17b]

Production of Hydrogen Chloride.—To a solution of aromatic compound at 25° in acetic acid in the dark was added a standard solution of chlorine. The mixture was set aside for more than twenty reaction half-lives. A rubber tube was then fitted round the neck of the flask and filled with water. The stopper was then carefully freed so that water filled the dead-space in the flask but no hydrogen chloride escaped. The whole solution was then added to water and titrated potentiometrically with silver nitrate. Anisole gave 1·00 mole of chloride per mole of chlorine consumed. Biphenyl (0·029, 0·057, 0·075, 0·100 mole) and chlorine (respectively 0·006, 0·006, 0·015, 0·020 mole) gave respectively 0·832, 0·823, 0·824, and 0·828 (mean 0·827) mole of chloride per mole of chlorine used up.

Possible Formation of Acetoxy-chloride Adducts.—Direct oxygen analysis of the organic product isolated from one of the above experiments showed that very little material ("acetoxy-chloride adduct") had been formed by addition of chlorine acetate (*e.g.*, by successive attachment of Cl^+ and OAc^-) to the aromatic nucleus. A separate test was carried out by refluxing the organic product, which had been carefully freed from acetic acid, with excess of sodium ethoxide. The solution was made just acid with 0·1N-sulphuric acid. Back-titration of an aliquot with 0·05N-sodium hydroxide to the end-point of Bromocresol Green–Methyl Red required 0·07 ml. of alkali. Back-titration to the phenolphthalein end-point of a second aliquot part which had been refluxed for 10 min. to remove dissolved carbon dioxide required 0·15 ml. of alkali. A control experiment in which β-hexachlorocyclohexane was used gave no significant difference between the titration to the two indicators, so it is concluded that the difference observed for the chlorinated product is experimentally significant and represents a titration of acetic acid; it corresponds with the production of *ca.* 2% of adduct, calculated as acetoxytrichlorotetrahydrobiphenyl, as a percentage of the chlorine used.

The crude chlorination product from biphenyl (30 g.) and chlorine (14 g.) in acetic acid was divided into three fractions by crystallisation from light petroleum. The most soluble fraction was dissolved in light petroleum and chromatographed on silica gel. 4-Chlorobiphenyl, 2-chlorobiphenyl, and biphenyl were eluted in that order with light petroleum. When these had been removed, the residue was eluted with ether. After the solvent had been removed, an oil (0·5 g., *ca.* 12% of the chlorinated material) was left. Several specimens of such material were rechromatographed; the product had the properties of a tetrachlorotetrahydrobiphenyl, as is shown by the following properties. Heating under reflux with an excess of sodium ethoxide gave 1·99 moles of hydrogen chloride per mole of adduct, calculated as $C_{12}H_{10}Cl_4$. Solvolysis in boiling 50% ethanol gave 0·78 mol. of acid after 9 hr., and 0·83 mol. after 18 hr. The ultraviolet absorption spectrum had a broad band with a maximum at 2500 Å (ε 9670, calc. as $C_{12}H_{10}Cl_4$) and a minimum at 2280 Å (ε 5410). The infrared spectrum had peaks (in the 650—1000 cm.$^{-1}$ region) at 954m, 917m, 868m, 821m, 773s, 757sh, 693s cm.$^{-1}$ (Found: C, 48·5; H, 3·4; Cl, 47·6. Calc. for $C_{12}H_{10}Cl_4$: C, 48·6; H, 3·4; Cl, 48·0%). Its rate coefficient for chlorination at 25° in acetic acid was $k_2 = 0{\cdot}007$ l. mole^{-1} min.$^{-1}$, about one sixth of that of biphenyl.

The product from treatment of the adduct with alkali was recovered (Found: C, 64·2; H, 3·8. Calc. for $C_{12}H_8Cl_2$: C, 64·6; H, 3·7%). It had infrared absorption bands at 875w, 854m, 820m, 811w, 799m, 757s, 693s, 684sh, s cm.$^{-1}$, and therefore appeared to be a mixture of 3,5- and 3,4-dichlorobiphenyl. This was confirmed by vapour-phase chromatography,

* This compound must be one of the major products of dichlorination of biphenyl; so we regard its identity as established by the vapour-phase chromatogram.

which showed that it contained dichlorobiphenyls in the following proportions: 3,5-, 59%; 3,4-, 33%; 2,4-, 6%; 2,5-, 2%. The last two isomers were separable only on a capillary column. There was also *ca.* 2% of material, the retention volume of which was consistent with its being a trichlorobiphenyl.

Neither the tetrachloride adduct nor more than a trace of dichlorobiphenyls was detected in the vapour-phase chromatograms of the products of chlorination of biphenyl with a deficiency of chlorine. The tetrachloride must, therefore, have a relatively high retention volume, and is not decomposed rapidly in the column. When, however, the crude product was distilled at ordinary pressure, the distillate contained increased amounts of 2,4(or 2,5)- and 3,4-dichlorobiphenyl; no significant amount of the 3,5-isomer was detected. Thermal decomposition of the tetrachloro-adduct must, therefore, give dichlorobiphenyls in proportions significantly different from those obtained by dehydrochlorination with alkali. This is not unexpected in view of the considerable difference in temperature and mechanism between the two reactions.

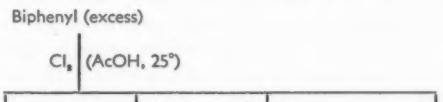
Discussion

The only product analysis previously recorded for the chlorination of biphenyl is that given by Jenkins, McCullough, and Booth [19] for chlorination of molten biphenyl at 90° with iron as a catalyst. The product was fractionally distilled; 36% of pure 2- and 29% of pure 4-chlorobiphenyl were isolated, and with reasonable assumptions concerning the composition of intermediate fractions, it can be estimated that there were formed 51% of 2-, 38% of 4-, and 12% of di- and poly-chlorobiphenyl ($\frac{1}{2}o : p$ 0·65—0·7).

In the present work, at a lower temperature, in acetic acid as solvent, the amount of *para*-substitution is about the same, but considerably less *ortho*-chlorobiphenyl is produced ($\frac{1}{2}o : p$ 0·31). This result has been confirmed by two independent methods of analysis, and there seems no reason to doubt its correctness under our experimental conditions.

We have been unable to detect 3-chlorobiphenyl in our products. Vapour-phase chromatography has been shown to detect easily the presence of 1% of this compound in a mixture with its isomers, so we feel confident that much less than this amount is present. This result is consistent with theoretical predictions based on the additivity principle. For, as has been shown elsewhere,[20] the 3-position in 4-acetamidobiphenyl is less reactive than the 2-position in acetanilide by a factor of 0·7; so, if this result can be carried over to the unsubstituted compound, the partial rate factor for *meta*-substitution in biphenyl is 0·7. From this and the total rate (422) of substitution relative to benzene,[8] the percentage of *meta*-substitution in biphenyl should be less than 0·06%.

The combined results for the analysis of reaction products by isotopic dilution, by vapour-phase chromatography, and by determination of hydrogen chloride liberated, and of the acetoxy-content of the isolated material, are summarised in the annexed chart.



Cl_2 consumed (moles %)	30	46·5	17·5	*ca.* 2
Biphenyl consumed (moles %)	34	54	9	*ca.* 1

Only small traces of other materials were detected in the vapour-phase chromatograms, and disubstitution by chlorine is small when biphenyl is present in the excess used in these experiments.

[19] Jenkins, McCullough, and Booth, *Ind. Eng. Chem.*, 1930, **22**, 31.
[20] de la Mare and Hassan, *J.*, 1958, 1519.

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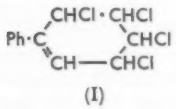
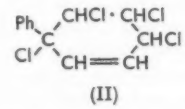
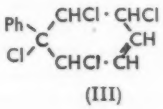
We have thus accounted in these experiments for about 96% of the total chlorine used; on a molar basis ~77% of the chlorine, and ~88% of the biphenyl, give products of substitution.

Of the chlorine consumed, ~17·5% gives an adduct, the major portion of which is a product in which two chlorine molecules have added to one ring of biphenyl. If stereoisomerism is neglected, the possible tetrachlorides are (I—III). Compounds (II) and


(I)


(II)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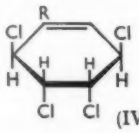

(IV)

(III) are probably at most minor components; for these materials, in which the double bond is not conjugated with the phenyl group, would not be expected to have intense absorption in the region of 2500 Å. 1-Phenylcyclohexene,[21] on the other hand, has $\varepsilon_{max.}$ 11,500 at 2470 Å, $\varepsilon_{min.}$ 4500 at 2250 Å, and the adduct has similar absorption ($\varepsilon_{max.}$ 9670 at 2500 Å; $\varepsilon_{min.}$ 5410 at 2280 Å).

The structure of the adduct can be further elucidated by consideration of the products obtained on reaction with alkali. Of the five known isomers of tetrachlorocyclohexene,[22] only one gives with alkali very little *p*-dichlorobenzene. This is the relatively unreactive α-isomer (IV; R = H). It seems likely that the phenyl group in the adduct would, if anything, favour the formation of a product containing *p*-chloro-substituents; so, since very little of this material (2,5-dichlorobiphenyl, 2%) was formed in the dehydrochlorination, we consider that structure (IV; R = Ph) represents the bulk of the adduct.

The rate of reaction of the adduct with alkali was also measured, and supports this view. For 0·00945M-$ArHCl_4$ and 0·0384M-sodium hydroxide in 80% ethanol at 30°, the plot of percentage reaction against time proceeded smoothly from the calculated initial titre to a value within 4% of the calculated infinity value. The rate-coefficient showed no significant change during the reaction; the second-order velocity coefficients, calculated by using the formula [23]

$$k_2 = \frac{2{\cdot}303}{t(B_0 - x)} \log_{10} \frac{x(B_0 - x)}{B_0(x_\infty - x)}$$

(where B_0 is the concentration of alkali at t_0, and x is the concentration of chloride liberated at time t), were 0·021 l. mole^{-1} sec.$^{-1}$ at 25% reaction and 0·024 l. mole^{-1} sec.$^{-1}$ at 80% reaction. So the reaction appears to characterise a single substance reacting with alkali to liberate the first chloride ion slowly and the second very rapidly. Three isomers of tetrachlorocyclohexene react more rapidly than this.* Since the inductive effect of the phenyl group would be expected to increase the rate of bimolecular elimination, the structure of the adduct can hardly accord with these. The two remaining isomers react more slowly than the adduct; the α-isomer has $k_2 = 0{\cdot}007$ l. mole^{-1} sec.$^{-1}$ at 28°; the δ-isomer has $k_2 = 0{\cdot}001$ l. mole^{-1} sec.$^{-1}$. The phenyl derivative of either of these would, it is thought, be more reactive, and the measured value for the adduct is in fact somewhat greater than that of the α-isomer of tetrachlorocyclohexene. So we regard the rate of reaction with alkali as evidence supporting our assignment of the structure of the adduct.

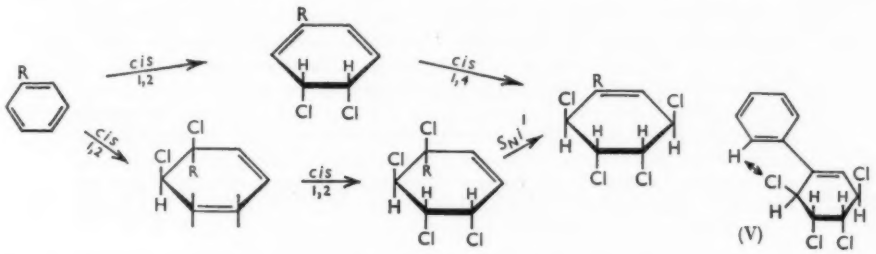
There are several theoretically possible ways in which the adduct could be formed. The routes indicated in the scheme involve *cis*-addition initiated at either the *para*- or

* The unknown structural isomer of tetrachlorocyclohexene and the two extra structural isomers possible for its 1-phenyl derivative would all be expected also to be quite reactive with alkali.

[21] Carlin and Landerl, *J. Amer. Chem. Soc.*, 1953, **75**, 3969; Baddeley, Chadwick, and Taylor, *J.*, 1956, 451.
[22] Orloff and Kolka, *J. Amer. Chem. Soc.*, 1954, **76**, 5484.
[23] Hughes, Ingold, and Pasternak, *J.*, 1953, 3832.

the *ortho*-position; they are mentioned because of the evidence [24] that *cis*-additions of chlorine are sometimes important under similar experimental conditions.

In a conformation (V) in which the phenyl group and the double bond are coplanar, the H–Cl distance (2·26 Å) marked by the arrow implies [25] an overlap of *ca.* 0·7 Å. Relief



of strain by rotation about the Ar–C bond may explain why the extinction coefficient for the adduct ($\varepsilon_{max.}$ 9670) is less than that of phenyl cyclohexene ($\varepsilon_{max.}$ 11,500). A rather more marked effect was noted by Carlin and Landerl [21] for a 6-methyl substituent.

The small reactivity of the adduct with molecular chlorine (in acetic acid at 25°, $k_2 = ca.\ 1 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$) may also partly reflect steric inhibition of conjugation. Such a compound might have been expected, by comparison of reactivities of cinnamyl chloride, allyl chloride, and 1,1-di(chloromethyl)ethylene,[26] to add chlorine at a rate of *ca.* 1 l. mole^{-1} sec.$^{-1}$; so it does not seem that such a low reactivity would be expected for the adduct from polar effects alone. A second, perhaps more important, factor may be that the 3-chlorine atom interferes sterically with the axial attack by the entering chlorine atom; a model shows that attack from the opposite side of the ring will be sterically impeded still more by the axial substituent on the 4- or 5-carbon atom.

It is possible also that the five large substituents attached to the cyclohexene ring in the adduct introduce enough conformational rigidity considerably to reduce the solvolytic reactivity of the 2- and the 5-chlorine substituent; the rate of solvolysis certainly seems rather less than would be expected for a cyclohex-2-enyl chloride,[27] even if allowance is made for the polar effects of the other chlorine atoms.

Analyses are partly by A. Bernhardt. We thank Drs. D. M. Hall and M. M. Harris for helpful suggestions, and Mr. P. J. Gaston and Mr. C. Bilby for technical assistance. Chromatographic separations on a capillary column, with photo-ionisation and electron-capture detectors, are by courtesy of Dr. J. E. Lovelock whom we thank also for valuable discussion.

Bedford College (University of London), Regent's Park, London, N.W.1.
Medical Research Council Laboratories, Holly Hill, London, N.W.3.
William Ramsay & Ralph Forster Laboratories,
University College London,
Gower Street, London, W.C.1. [*Received, January 11th,* 1961.]

[24] de la Mare and Klassen, *Chem. and Ind.*, 1960, 498.
[25] Maccoll, in "Progress in Stereochemistry" (ed. Klyne), Butterworths, London, 1953, p. 361.
[26] de la Mare, *Quart. Rev.*, 1948, **3**, 126.
[27] Goering, Nevitt, and Silversmith, *J. Amer. Chem. Soc.*, 1955, **77**, 5026.

XUM

538. *Gas-phase Eliminations. Part II.* The Pyrolysis of s-Butyl Chloride, and the Direction of Eliminations from s-Butyl Compounds.†*

By Allan Maccoll and R. H. Stone.

The pyrolysis of s-butyl chloride has been shown to be a homogeneous unimolecular process at 330—390°, producing hydrogen chloride and a mixture of isomeric butenes. The Arrhenius parameters (log A 13·62; E 49·6 kcal./mole) are compared with recorded values for other secondary halides, verifying a common mechanism for all. Vapour-phase chromatography has been used to determine the composition of the mixture of butenes produced by unimolecular elimination from s-butyl chloride, bromide, iodide, and acetate. Catalysis of the transformation but-1-ene ⇌ but-2-ene by hydrogen halides and by iodine has been observed. The results are discussed in the light of current theories of reactivity.

In investigating factors influencing the direction of elimination, it is desirable to work with a series of compounds for which the mechanism of elimination has been established. Such a series, the simplest of its type, involving β-methylation, is provided by the s-butyl compounds, elimination from which is homogeneous and unimolecular and follows the stoicheiometric scheme:

$$C_4H_9X \begin{cases} \nearrow CH_3{\cdot}CH{:}CH{\cdot}CH_3 \\ \searrow CH_3{\cdot}CH_2{\cdot}CH{:}CH_2 \end{cases} + HX$$

with X = Cl, Br, I, or OAc. Vapour-phase chromatography affords a simple technique for separating the three olefinic products, but-1-ene and *cis*- and *trans*-but-2-ene. Two extreme types of elimination have long been recognized,[1] Saytzeff, leading to the most highly alkylated ethylene, and Hoffman, leading to the least alkylated ethylene. The former is characteristic of the $E1$ reaction of alkyl halides, and the latter of the $E2$ reaction of alkylsulphonium salts, in ionising solvents. The present investigation takes on a special interest in view of the analogy that has been proposed [2] between gas-phase eliminations and reactions in polar solvents. After recording the kinetics of the pyrolysis of s-butyl chloride, this paper describes the direction of elimination from s-butyl halides and s-butyl acetate.

The Pyrolysis of s-Butyl Chloride.—The reaction was studied by a static method in a reaction vessel seasoned with the products of the decomposition of allyl bromide, by measuring the rate of pressure increase.[3] That the stoicheiometry is well represented by the equation, $C_4H_9Cl \longrightarrow C_4H_8 + HCl$, follows from two pieces of evidence. First, no permanent gases or hydrocarbons other than the butenes were observed in the products. And, secondly, the ratio of final (p_t) to initial (p_0) pressure approached the theoretical value of 2, the mean value being 1·93 (Table 1). In view of this and of the clean nature of the elimination for other alkyl chlorides,[4,5] it was not deemed necessary further to check the stoicheiometry.

That the reaction is of the first order follows from the linearity of the plots of log $(2p_0 - p_t)$ against t, and from the lack of dependence of the first-order rate coefficients

* Part I, Maccoll, *J.*, 1958, 3398.

† For a preliminary account see Kekulé Symposium on Theoretical Organic Chemistry, Butterworths, London, 1959.

[1] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953.
[2] Maccoll and Thomas, *Nature*, 1955, **176**, 392.
[3] Maccoll, *J.*, 1955, 965.
[4] Barton and Howlett, *J.*, 1949, 155; Barton, Head, and Williams, *J.*, 1951, 2039; Howlett, *J.*, 1952, 4487; Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725; Brearley, Kistiakowsky, and Stauffer, *J. Amer. Chem. Soc.*, 1936, **58**, 43; Swinbourne, *Austral. J. Chem.*, 1958, **11**, 314.
[5] Barton and Head, *Trans. Faraday Soc.*, 1950, **46**, 114.

on initial pressure (Table 2). Results at various temperatures confirmed this conclusion and so first-order constants were calculated for all the runs. The temperature-dependence

TABLE 1.

Temp. (c)	391·3°	372·3°	356·2°	332·6°	329·8°
p_0 (mm.)	280	254	132	187	340
p_i/p_0	1·93	1·92	1·89	1·94	1·97

TABLE 2. *Rate coefficients, at* 356·8° C.

p_0 (mm.)	155·0	335·0	408·0	490·0
10^5k_1 (sec.$^{-1}$)	27·6	28·5	28·5	27·2

of the rate constants in the range 330—390° is shown in Table 3. These values lead to the Arrhenius equation

$$k_1 \text{ (sec.}^{-1}) = 4{\cdot}14 \times 10^{13} \exp(-49{,}600/RT)$$

which fitted the experimental results very well.

TABLE 3. *Temperature dependence.*

Temp.	391·3°	372·3°	363·6°	360·2°	356·8°	342·6°	329·8°
10^5k_1 (sec.$^{-1}$)	191	63·5	39·7	29·4	28·0	10·2	3·87
No. of runs	6	8	6	5	4	4	3

In determining the mechanism of the reaction, it remained to verify its homogeneity and to test for a chain mechanism by the use of an inhibitor. To check the homogeneity, runs were carried out in a reaction vessel packed with glass tubing to give a surface–volume ratio increased by a factor of 6. The results (Table 4) show a 20% increase in the mean rate constant ($25{\cdot}2 \times 10^{-5}$ sec.$^{-1}$). In view of the large increase in surface–volume ratio, it may be concluded that the reaction is homogeneous. The inhibitor chosen was cyclohexene, which has been proved [6] to be very efficient in inhibition studies in the bromide series. Table 5 shows the effect of different ratios of inhibitor to substrate partial pressures (p_i/p_0). The mean value for the runs in the presence of varying partial pressures of cyclohexene is $14{\cdot}6 \times 10^{-5}$ sec.$^{-1}$ which is close to the value $14{\cdot}7 \times 10^{-5}$ sec.$^{-1}$, observed for the substrate alone. Chain mechanisms thus appear to play little part in the decomposition.

TABLE 4. *Reaction at higher surface–volume ratio, at* 354·2°.

p_0 (mm.)	149	169	165	173	250	290
10^5k_1 (sec.$^{-1}$)	29·1	24·6	26·6	22·6	22·1	26·4

TABLE 5. *Effect of inhibitor, at* 350°.

p_i/p_0	0·17	0·60	0·66	0·83	1·05
p_0 (mm.)	237	195	191	181	185
10^5k_1 (sec.$^{-1}$)	14·8	14·4	14·5	14·7	14·7

It may be concluded that s-butyl chloride decomposes by a homogeneous, unimolecular reaction into a mixture of butenes and hydrogen chloride. This is in line with the behaviour of other alkyl chlorides studied by Barton, Howlett, and their co-workers. The Arrhenius parameters for a series of i-propyl and s-butyl halides are shown in Table 6, together with the relative rates for the series chloride, bromide, and iodide and for i-propyl/s-butyl, the temperature being chosen in each case such that the smaller rate constant has the value of 10^{-4} sec.$^{-1}$. Comparisons of the ratios given confirm a common mechanism for all the compounds.

An interesting point arises as to the effect of β-methylation, which may either be a

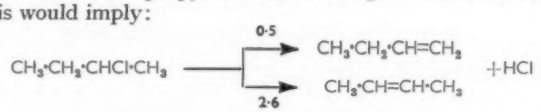
[6] Maccoll and Thomas, *J.*, 1957, 5033.

first-order effect on the β-carbon–hydrogen bond, or a second-order effect on the α-carbon–chlorine bond. If the former is true, the increase in rate in going from i-propyl to s-butyl chloride should be due entirely to elimination towards the centre of the molecule, resulting

TABLE 6. *Some relative pyrolysis rates.*

	Chloride [5]		Bromide [7]		Iodide [8]	
	Pr^i	Bu^s	Pr^i	Bu^s	Pr^i	Bu^s
log *A*	13·40	13·62	13·62	13·53	14·49	14·90
E (kcal. mole^{-1})	50·5	49·6	47·8	46·5	48·0	47·9
k_{Pr^iX}/k_{Pr^iCl} (360·8°)	1		13·5		89	
k_{Bu^sX}/k_{Bu^sCl} (343·4°)	1		11·5		85	
k_{Bu^sX}/k_{Pr^iX}	3·1 (360·8°)		3·5 (319·1°)		2·8 (294·0°)	

in but-2-ene. Thus, at 361°, if i-propyl chloride is assigned a rate of 1, that of s-butyl chloride is 3·1. This would imply:



and the ratio of but-1-ene to but-2-ene should be 1 : 5·2, giving 84% of but-2-ene. Analysis of the product mixture gives 60% of but-2-ene (see below). The effect of the β-methyl group thus appears to be predominantly a second-order effect on the carbon–chlorine bond. The effect is analysed in a different fashion in Table 7, which shows that the added methyl group not only increases the rate of elimination in the branch to which it is added, but also in the branch which is unchanged. This type of behaviour has earlier been noted by Ingold [1] for t-butyl and t-pentyl halides undergoing elimination by the *E*1 mechanism in a polar solvent. Further evidence of the second-order nature of the effect of β-methylation comes from work by Wong [9] on the series Me_2CClR, with R = Me, Et, Pr^i, and Bu^t. The rate of elimination progressively increases with β-methylation, despite the fact that in the last compound elimination is of necessity entirely in the shorter branch.

TABLE 7. *Directions of reaction, at* 361°.

Rate per branch	Chloride used	Rate per branch
0·5	$CH_3·CHCl·CH_3$	0·5
1·83	$CH_3·CH_2·CHCl·CH_3$	1·24

Direction of Elimination from s-Butyl Compounds.—When an equilibrium exists between the products of a given reaction, the reaction may be determined by (*a*) thermodynamic or (*b*) kinetic considerations. In the former case the equilibrium proportions of the products would be expected; in the latter, proportions away from the equilibrium ones, followed by a slow approach to equilibrium. For this reason, it is important to show, in the case

TABLE 8. *Composition of products.*

Temp.	276·8°	331·8°	356·8°	381·8°	406·8°	431·8°
But-1-ene (%)	12·6	13·6	14·9	16·0	17·3	18·3
trans-But-2-ene (%)	55·2	54·1	52·8	52·0	50·8	49·7
cis-But-2-ene (%)	32·2	32·2	32·2	32·1	32·0	31·8

where kinetic control is suspected, that the half-life of isomerisation is very much greater than the half-life of the elimination. The equilibrium proportions of the various isomeric butenes, computed from the data in the literature,[10] are shown in Table 8, over the relevant temperature range.

[7] Maccoll and Thomas, *J.*, 1955, 979, 2445.
[8] Holmes and Maccoll, *Proc. Chem. Soc.*, 1957, 175; Holmes, Ph.D. Thesis, London, 1957.
[9] Wong, Ph.D. Thesis, London, 1958.
[10] "Selected Values of the Physical and Thermodynamic Properties of Hydrocarbons," Carnegie Press, Pittsburgh, 1953.

In order to verify that the rate of isomerisation was slow, a number of experiments were carried out with the pure butenes. The following observations were made at 342·8°. (1) In a clean vessel, the *cis–trans*-equilibrium was readily attained, but no isomerisation from but-1-ene to but-2-ene or *vice versa* could be observed during 1 hour. (2) In a carbon-coated vessel, *cis–trans*-isomerisation was even more rapidly attained than in a clean vessel, but no but-1-ene was formed from but-2-ene in 4 hr. However, about 2% of but-2-ene was formed from but-1-ene in the time. (3) The approach to equilibrium between but-2-ene and but-1-ene was markedly catalysed by hydrogen chloride, hydrogen bromide, and iodine.

In the investigation of catalysis by hydrogen halide and iodine, the catalyst was produced by decomposing the appropriate i-propyl compound in the presence of but-1-ene. The amount of hydrogen halide or iodine produced could be estimated from the area of the propene peak on gas–liquid chromatography. The results, shown in Table 9, clearly indicate catalysis by the hydrogen halides and by iodine, the catalytic efficiency being in the order iodine > hydrogen bromide > hydrogen chloride. However, it may be inferred that the rates are slow compared with the rate of decomposition of the secondary butyl halide, at the temperatures used for the investigation of the products. When acetic acid was used as catalyst, no isomerisation of but-1-ene was observed.

TABLE 9. *Effect of catalysts.*

	Catalyst: hydrogen chloride. Temp. 342·8°.				
Reaction time (hr.)	4	4	18	16	
Mol. ratio,* acid : butene	0	0·30	0·75	2·00	
Isomerisation (%)	2	2	33	70	
	Catalyst: hydrogen bromide. Temp. 342·8°.				
Reaction time (hr.)	2	1·5	18		
Mol. ratio,* acid : butene	0·5	2·0	2·0		
Isomerisation (%)	16	70	82 (equil.)		
	Catalyst: iodine. Temp. 353·8°				
Reaction time (hr.)	1	1	1	0·67	0·50
Mol. ratio,* acid : butene	0·9	1·1	1·3	1·4	3·7
Isomerisation (%)	69	75	79	63	69

* Obtained at the moment of sampling.

TABLE 10. *Product analyses*

	s-Butyl chloride.							
Temp.	291·3°	372·3°	363·6°	360·2°	356·8°	342·6°	329·8°	
But-1-ene (%)	41·7	30·2	40·5	38·1	42·9	37·3	41·2	
cis-But-2-ene (%) *	37·5	36·4	38·9	40·6	35·6	38·5	36·7	
	s-Butyl bromide.							
Temp.	387·6°	382°	357·8° †	345·8°	350° †	349·8°	344·2°	
But-1-ene (%)	27·6	25·0	22·7	23·7	24·0	24·8	26·2	
cis-But-2-ene (%) *	33·9	38·6	41·3	37·9	40·0	35·4	36·6	
Temp.	341·1°	341·1° †	333·3°	322·2°	320·4°	309·4° †	289·1°	289·1° †
But-1-ene (%)	23·2	22·6	22·0	21·3	23·2	24·0	19·6	18·4
cis-But-2-ene (%) *	36·3	39·0	39·9	36·9	38·2	40·5	39·4	41·2
	s-Butyl iodide.				*s-Butyl acetate.*			
Temp.	312·6°	297·7°	273·9°	339°	321°	318°	316·8°	
But-1-ene (%)	17·5	15·5	17·3	53·4	54·1	54·0	53·6	
cis-But-2-ene (%) *	37·0	37·3	37·4	35·9	36·3	33·7	37·5	

* *cis*-Butene is cited as a percentage of the total but-2-ene.

† These runs were done with cyclohexene as an inhibitor (Kale, Maccoll, and Thomas, *J.*, 1958, 2016).

In analyses of the products, the reaction time used was approximately the half-life. The results are shown in Table 10.

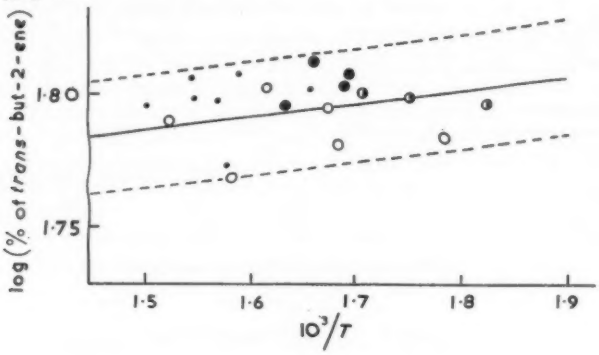
In order to reduce the catalysis by hydrogen halides, some experiments were carried out in the presence of ammonia. It was expected that the ammonia would condense as the ammonium halide, in the cool dead-space, thus at least partially removing hydrogen halide from the system. The results for s-butyl chloride and bromide are shown in Table 11. Comparison of Tables 10 and 11 suggests that catalysis by hydrogen halide

TABLE 11. *Pyrolyses in presence of ammonia.*

	s-Butyl chloride (temp. 354°)			*s*-Butyl bromide (temp. 342·60)		
Init. press. of halide (mm.)	109	110	107	109·5	110·5	108·0
Press of ammonia (mm.)	188·5	100	50·7	157·2	104	52·5
But-1-ene (%)	41·7	42·0	40·9	36·2	34·3	32·5

has little effect in the case of s-butyl chloride, but an appreciable effect in the case of s-butyl bromide. From the reported values, it is suggested that the best values for the percentage of but-1-ene produced by gas-phase elimination from the appropriate s-butyl compound are as shown in Table 12. While the figures for the acetate [11] and chloride are considered

The logarithm of the percentage of trans-*but-2-ene in the total but-2-ene as a function of* T^{-1}. *Chlorides* •, *bromides* ○, *iodides* ◑, *acetates* ●. *The full line gives the equilibrium values; the broken lines represent* ±5% *of these.*



to be a reliable representation of the products produced at the instant of reaction, it is possible that the bromide figure is somewhat low because of subsequent catalysed rearrangement; the iodide figure is almost certainly low.

TABLE 12. *Best values for pyrolysis.*

Compound	Acetate	Chloride	Bromide	Iodide
But-1-ene (%)	54	40	34	17

It can be concluded from the figures in Table 10 for the amount of *cis*-but-2-ene that, under the conditions of the present experiments (carbon-coated vessels and the presence of hydrogen halide or iodide), the *cis–trans*-equilibrium is rapidly attained. This is shown in the Figure where the log of the percentage of *trans*-but-2-ene is plotted against T^{-1}. The full line represents the equilibrium value, and the broken lines ±5% deviations. *All the experimental points lie within these limits.* That this is also true for the acetate

[11] Cf. Froemsdorf, Collins, Hammond, and DePuy, *J. Amer. Chem. Soc.*, 1959, **81**, 643; Haag and Pines, *J. Org. Chem.*, 1959, **24**, 877.

suggests that the carbonaceous surface is the more important factor in establishing the equilibrium. It is worthy of note that if planarity or near-planarity is required in the transition state for elimination then the *trans*-form will be favoured. But, as has been seen earlier (Table 8), this is also the form that is favoured by thermodynamic stability.

Experimental

s-Butyl chloride was prepared by shaking a commercial sample with hydrochloric acid, then with 5% sodium hydrogen carbonate solution and with water, drying ($CaCl_2$), and distillation through a 1-m. column packed with glass helices. The physical constants were: b. p. 68·1°/750 mm., n_D^{25} 1·3944 (lit.,[12] 68·25°/760 mm., 1·3946). s-Butyl bromide, treated in the same fashion as the chloride, with substitution of hydrobromic acid for hydrochloric acid, had b. p. 91·1°/756 mm., n_D^{25} 1·4341 (lit.,[13] 91·2°/750 mm., 1·4342). A newly obtained commercial sample of s-butyl iodide was left over silver powder for several days and then distilled from silver powder, through a short column; it had ("lit." below denotes ref. 12) b. p. 119·5°/737 mm., n_D^{25} 1·4971 (lit., 120·0°/760 mm., 1·4975). The isopropyl halides, used only in the isomerisation experiments, after purification had the physical constants: chloride, b. p. 39·0°/766 mm., n_D^{25} 1·3750 (lit., 38·4°/760 mm., n_D^{25} 1·3755); bromide, b. p. 59·5°/765 mm., n_D^{25} 1·4224 (lit., 59·35°/760 mm., 1·4228); iodide, b. p. 89·7°/761 mm., n_D^{25} 1·4959 (lit., 89·45°/760 mm., 1·4970). A commercial sample of cyclohexene was shaken with sodium hydrogen sulphite solution, dried ($CaCl_2$), and distilled in an atmosphere of nitrogen; it had b. p. 83·0°/760 mm., n_D^{25} 1·4435 (lit., 82·8°/760 mm., 1·4437).

The apparatus and techniques used for the kinetic investigation were essentially the same as those described earlier.[3]

The gas-chromatographic column was 20 ft. long, packed with a 2 : 3 w/w mixture of ethyl acetoacetate and Celite 545. The column was cooled to 4°; nitrogen was used as the carrier gas; and detection was by means of a katharometer and recorder. The apparatus was calibrated with pure butenes, obtained from the Chemical Research Laboratory, and checked by analysis of an equimolar mixture of butenes. The mean of the results of eight determinations gave but-1-ene 32·8, *trans*-but-2-ene 33·4, and *cis*-but-2-ene 33·6%. The analysis was based on area measurements (peak height × 0·5 peak width), and it was concluded that no corrections for differences in thermal conductivity were necessary.

The authors thank Dr. E. U. Emovon for the products from some of his kinetic studies which were used to get the isomeric composition of the butenes produced in the pyrolysis of s-butyl acetate. They also thank Mr. R. C. Bicknell for doing the inhibited runs with s-butyl chloride.

William Ramsey and Ralph Forster Laboratories,
University College, Gower Street,
London, W.C.1.

[*Received, December 1st*, 1960.]

[12] Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950.
[13] Heston, Hennelly, and Smyth, *J. Amer. Chem. Soc.*, 1950 **72**, 2072.

539. *Cyclic Diarsines. Part VI.*[1] *The Thermal Decomposition of Some Cyclic Quaternary Diarsonium Dihydroxides and Dibromides.*

By M. H. Forbes, Denys M. Heinekey, Frederick G. Mann, and Ian T. Millar.

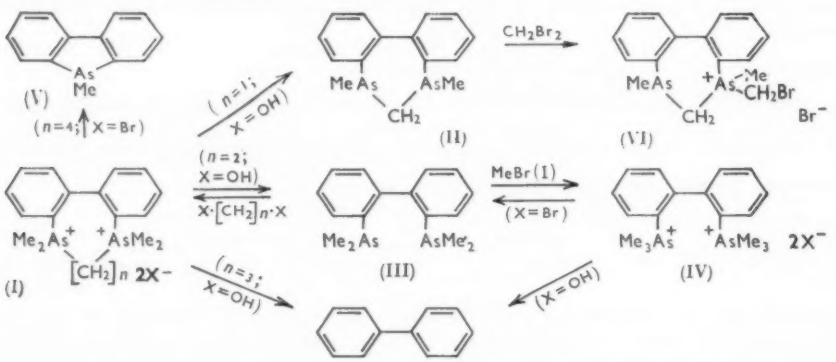
The thermal decomposition of some cyclic quaternary diarsonium dihydroxides (I; $n = 1$, 2, or 3; X = OH), derived from 2,2′-biphenylylenebisdimethylarsine (III), has been found to proceed in a manner markedly dependent on the value of n. When $n = 1$, the arsenical product is 5,7-dimethyl-5,7-diarsa-1,2:3,4-dibenzocycloheptadiene (II); when $n = 2$, the diarsine (III) results; when $n = 3$, thermal decomposition yields biphenyl, which is also obtained by heating the dimethohydroxide (IV; X = OH) of the diarsine (III).

The thermal decomposition of certain diarsonium dibromides derived from 2,2′-biphenylylenebisdimethylarsine, and a brief investigation of the quaternising properties of the nitrogen analogue of this diarsine, 2,2′-bisdimethylaminobiphenyl, are described; the preparation and nuclear magnetic resonance characteristics of some quaternary arsonium bromides having a vinyl group attached to arsenic are also noted.

In Part V, the formation and thermal decomposition of some cyclic diarsonium dibromides derived from 2,2′-biphenylylenebisdimethylarsine (III) by diquaternisation with, *e.g.*, methylene, ethylene, and trimethylene dibromides, giving dibromides (I; $n = 1$, 2, and 3 respectively; X = Br), were described.[1] We have now investigated the thermal decomposition of the corresponding dihydroxides.

In contrast with the thermal decomposition of quaternary arsonium halides, that of quaternary arsonium hydroxides has been little investigated. Michaelis[2] reported that methyltriphenylarsonium hydroxide decomposes at 100° to give triphenylarsine and methanol.

The dihydroxide (I; $n = 1$; X = OH), when heated at 150°/0·01 mm. under nitrogen, decomposes smoothly to give the diarsine (II), behaviour resembling that of Michaelis's hydroxide: it is noteworthy that the diarsine (II) is similarly formed by the thermal decomposition of the dibromide (I; $n = 1$; X = Br).[1]



Thermal decomposition of the dihydroxides (I; $n = 2$ or 3; X = OH) is of particular interest, since the corresponding dibromides (I; $n = 2$ or 3; X = Br) decompose with contraction of the heterocyclic rings to give 9-methyl-9-arsafluorene (V).[1] We find that

[1] *Part V, Heaney, Heinekey, Mann, and Millar, J., 1958, 3838.*
[2] Michaelis, *Annalen*, 1902, **321**, 166.

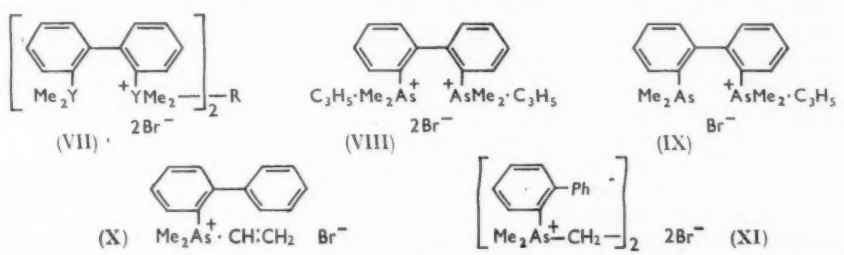
the diarsonium dihydroxide (I; $n = 2$; X = OH) decomposes smoothly at 160°/0·05 mm., giving 2,2′-biphenylylenebisdimethylarsine (III). When, however, the dihydroxide (I; $n = 3$; X = OH) was heated at 165°/0·5 mm., the only product identified was biphenyl; this is also a product of the thermal decomposition of 2,2′-biphenylylenebisdimethylarsine dimethohydroxide (IV; X = OH).

In view of the novel mode of thermal decomposition displayed by the cyclic diarsonium dibromides (I; $n = 2$ or 3; X = Br), the formation and thermal decomposition of certain other cyclic and non-cyclic diarsonium dibromides derived from 2,2′-biphenylylenebisdimethylarsine (III) have been investigated.

Ethylidene dibromide, unlike methylene dibromide, fails to give a heterocyclic diquaternary salt with 2,2′-biphenylylenebisdimethylarsine, giving instead ethylidenebis(2′-dimethylarsino-2-biphenylyldimethylarsonium) dibromide (VII; Y = As, R = >CHMe).

2,2′-Biphenylylenebis(allyldimethylarsonium) dibromide (VIII), prepared from 2,2′-biphenylylenebisdimethylarsine and allyl bromide, decomposes at 250°/0·05 mm. to give 2,2′-biphenylylenebisdimethylarsine (III). (The dimethiodide[3] and dimethobromide of this diarsine decompose similarly to regenerate the diarsine.) This decomposition almost certainly involves the intermediate formation of the monoquaternary bromide (IX); it is therefore unlikely that thermal decomposition of the dibromide (I; $n = 3$; X = Br) to 9-methyl-9-arsafluorene (V) occurs by initial fission of the ring with β-elimination of hydrogen bromide to give the bromide (IX) followed by further elimination and ring-closure to give the arsafluorene (V).

5,5,10,10-Tetramethyl-5,10-diarsonia-1,2:3,4-dibenzocyclodecadiene dibromide (I; $n = 4$; X = Br), prepared from 2,2′-biphenylylenebisdimethylarsine and 1,4-dibromobutane, decomposes when heated, with contraction of the ten-membered heterocyclic ring, giving a mixture of 9-methyl-9-arsafluorene (V) and 9-bromo-9-arsafluorene; it thus resembles the similar dibromides in which $n = 2$ or 3. It has previously been noted that in such



quaternary diarsonium dibromides the arsonium groups are bridged by a flexible carbon chain which also bears hydrogen in the β-relation to the arsenic atoms, and this may be significant in their decomposition with ring contraction. In the hope of testing whether the second of these conditions is necessary for the formation of a 9-arsafluorene, attempts were made to quaternise 2,2′-biphenylylenebisdimethylarsine with 1,3-dibromo-2,2′-dimethylpropane, $CH_2Br{\cdot}CMe_2{\cdot}CH_2Br$: the resulting diarsonium dibromide would possess a flexible alkylene bridge, lacking β-hydrogen atoms. As a neopentyl-type halide, 1,3-dibromo-2,2-dimethylpropane was expected to show only very low reactivity as a quaternising agent; it failed to give a dinitrile with potassium cyanide.[4] It required heating with the diarsine at 125° in the presence of methanol for some days for quaternisation to occur; the resulting salt was found to be identical with the dimethobromide (IV; X = Br) of the diarsine (III), as shown by examination of the melting point (alone and mixed), infrared absorption, and analytical composition of specimens prepared by each

[3] Heaney, Mann, and Millar, *J.*, 1957, 3930.
[4] Franke, *Monatsh.*, 1913, **34**, 1893.

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route, and of the corresponding picrates. Although it was recognised that a system containing the diarsine, 1,3-dibromo-2,2-dimethylpropane, and methanol was potentially complex, since elimination and rearrangement might occur under the forcing conditions required for quaternisation, the formation of the salt (IV; X = Br) is noteworthy.

In order to throw light on the origin of the 9-methyl group in arsafluorenes formed by the thermal decomposition of the dibromides (I; $n = 2$, 3, or 4; X = Br), 2,2′-biphenylylenebisdiethylarsine, prepared from 2,2′-dilithiobiphenyl and chlorodiethylarsine, was heated with ethylene dibromide. However, it is doubtful if cyclising diquaternisation to give the tetraethyl analogue of (I; $n = 2$; X = Br) occurred to any large extent, for the product was a mixture from which no single quaternary salt could be isolated. This marked difference in behaviour between the bisdimethyl- and the bisdiethyl-arsine is probably caused by the greater steric hindrance in the latter.

Attempts to construct "Catalin" models of salts derived from the cyclic diarsine (II) by further cyclising diquaternisation with αω-alkylene dihalides suggest that such bridging of the arsenic atoms would be stereochemically unlikely. In accord with this prediction, it was found that the diarsine (II), even when treated with methylene dibromide under forcing conditions, gave only the monoquaternary salt (VI) and not the isomeric doubly bridged dibromide. In addition to the stereochemical difficulty of further quaternisation to give the latter salt, it is clear that deactivation of the tertiary arsine group by the arsonium group resulting from initial monoquaternisation, transmitted through both the biphenyl system and the single methylene group, is probably marked in the bromide (VI).

We have prepared triethylvinylarsonium bromide and 2-biphenylyldimethylvinylarsonium bromide (X) in order both to recognise the ·CH:CHAs group by nuclear magnetic resonance spectra, and to establish the absence of this group in the foregoing heterocyclic diarsines, since the small scale of the early experiments on the thermal decomposition of the compound (I; $n = 2$; X = OH) and the difficulty of purification of the resulting diarsine and its quaternary salts made it initially seem possible that the thermal decomposition product might be 5,8-dimethyl-5,8-diarsa-1,2:3,4-dibenzocyclo-octa-1,3,6-triene. Triethylvinylarsonium bromide was readily prepared by interaction of equimolecular quantities of triethylarsine and ethylene dibromide to give 2-bromoethyltriethylarsonium bromide which on treatment with silver oxide in aqueous solution, followed by filtration and neutralisation with hydrobromic acid, gave the vinylarsonium bromide.

Considerable care was required, however, in the preparation of 2-biphenylyldimethylvinylarsonium bromide (X). When an equimolecular mixture of 2-biphenylyldimethylarsine and ethylene dibromide was heated under nitrogen at 100° for 6 hr., the only crystalline product was ethylenebis-(2-biphenylyldimethylarsonium) dibromide (XI), which has a very low solubility in ethanol. When, however, a mixture of the arsine and an excess (3·75 mols.) of ethylene dibromide was heated at 50° for 72 hr., it afforded the required 2-bromoethyl-2-biphenylyldimethylarsonium bromide, which was readily purified by utilising its high solubility in ethanol. This salt, when treated as before with silver oxide and then hydrobromic acid, gave 2-biphenylyldimethylvinylarsonium bromide (X).

Nuclear magnetic resonance spectra of hydrogen nuclei were obtained at 40 Mc. by using a Varian Associates 4300B spectrometer and 12″ electromagnet, with flux stabilisation and sample spinning. Positions of the resonances are quoted as chemical shifts on the tetramethylsilane scale. The τ values for the D_2O solutions were measured by using t-butyl alcohol as a subsidiary internal standard. The following values were obtained for the above vinylarsonium bromides and for tri-2-chlorovinylarsine:

Compound	Solvent	τ
$[Et_2As{\cdot}CH{:}CH_2]Br$	D_2O	3·47
$[C_{12}H_8{\cdot}AsMe_2{\cdot}CH{:}CH_2]Br$	D_2O	3·34, 3·11
$As(CH{:}CHCl)_3$	CCl_4	3·62

The presence of the ·CH: group directly linked to the arsenic atom can thus be clearly detected. It could not be similarly detected in the dibromide (I; $n = 2$; X = Br), or the diarsine (III) or its dimethobromide.

The ultraviolet absorption spectra of certain of the above arsonium salts and of 5,10-dimethyl-5,10-diarsa-1,2:3,4:7,8-tribenzocyclodecatriene dimethobromide[1] are recorded in Figs. 1 and 2. The broad absorption centred at 317 mμ ($\log_{10}$ ε 3·403) in the spectrum of the methiodide of the arsafluorene (V) (Fig. 1, C) has no counterpart in this region in the spectra of any other of these arsonium salts, and is probably to be attributed to the central 5-membered monoarsine ring system.

The optical resolution of the four cyclic diarsonium salts (Fig. 2) will be described in another paper.

2,2′-Biphenylylenebisdimethylamine was first prepared by Shaw and Turner,[5] who

FIG. 1. FIG. 2.

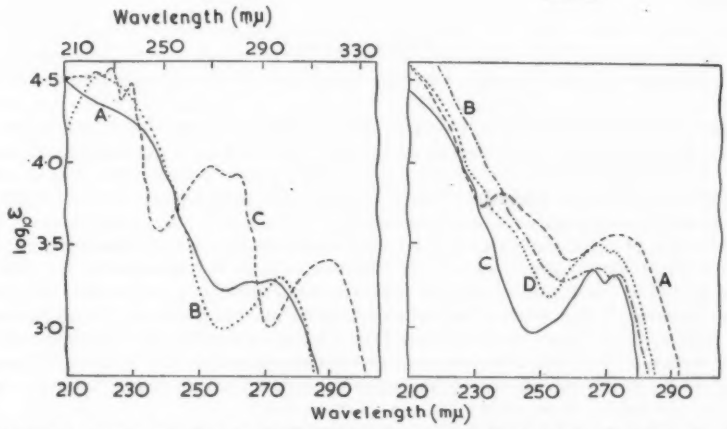

FIG. 1. *Ultraviolet spectra of* 2-*biphenylyl-dimethylarsine methiodide* (A), 2,2′-*biphenylylenebisdimethylarsine dimethiodide* (IV; X = I) (B), *and* 9-*methyl-9-arsafluorene methiodide* (C) (*all in water*). *The lower scale of* mμ *values applies to* (A) *and* (B), *and the upper scale to* (C). (*The iodide ion has an absorption band at* 225 mμ, *of peak-height* $\log_{10}$ ε 4·017, *and of half-width* 22 mμ.)

FIG. 2. *Ultraviolet spectra of* 5,7-*dimethyl-5,7-diarsa-*1,2:3,4-*dibenzocycloheptadiene dimethobromide* (I; $n = 1$, X = Br) (A), 5,8-*dimethyl-5,8-diarsa-*1,2:3,4-*dibenzocyclo-octadiene dimethobromide* (I; $n = 2$, X = Br) (B), 5,9-*dimethyl-5,9-diarsa-*1,2:3,4-*dibenzocyclononadiene dimethobromide* (I; $n = 3$, X = Br) (C), *and* 5,10-*dimethyl-5,10-diarsa-*1,2:3,4:7,8-*tribenzocyclodecatriene dimethobromide* (D) (*all in water*).

found that it forms a monohydriodide and monomethiodide, and established the non-planarity of the biphenyl system in the cation of the latter salt by resolving it. This di(tertiary amine) would be expected to show the effect of inhibition of basicity at one basic centre as a result of salt formation at the other, an effect shown, *e.g.*, by the arsenic analogue, 2,2′-biphenylylenebisdimethylarsine.[1] Such inhibition of basicity in the diamine might be expected to be not much greater than in the diarsine (which under very mild conditions undergoes monoquaternisation with methyl bromide but readily diquaternises with methyl iodide) since a unit positive pole is involved in both cases, and non-planarity in the biphenyl system, which might affect mesomeric transmission of the effect, would be comparable in the two cases. However, a " Catalin " model of the cation of 2′-dimethylamino-2-biphenylyltrimethylammonium iodide reveals that the formation of a dimethiodide would be very difficult; owing to the comparatively small size of the nitrogen atoms, the attachment of a second methyl group to form the dimethiodide is impeded

[5] Shaw and Turner, *J.*, 1933, 135.

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by steric overcrowding about the nitrogen atom. This effect is less marked in the analogous di(tertiary arsine) since the larger arsonium ion holds the attached groups at greater distances, and the overcrowding effect is reduced. Moreover, a " Catalin " model can be made for the product of cyclic diquaternisation of the diamine with an alkylene dibromide, $Br\cdot[CH_2]_n\cdot Br$, when $n = 1$, but not when $n = 2$—6 or when the bridge is *o*-xylylene, implying steric hindrance to such diquaternisations. When the diamine is heated with an excess of methyl iodide in the presence of methanol or nitromethane (both promoters of quaternisation) for a prolonged period, only the monomethiodide is formed. Similarly, vigorous treatment of the base with ethylene dibromide results only in monoquaternisation, giving ethylenebis-(2′-dimethylamino-2-biphenylyldimethylammonium) dibromide, (VII; Y = N, R = $\cdot CH_2\cdot CH_2$). Similar treatment of the diamine with methylene dibromide failed to give evidence of salt formation, a result indicating either lower reactivity or greater steric obstruction of the group $\cdot CH_2Br$ than of $\cdot CH_2\cdot CH_2Br$.

Experimental

Compounds are colourless unless otherwise described. M. p.s were determined on a Kofler hot stage.

The quaternary dihydroxides described below, when isolated by evaporation of their solutions, were hygroscopic glassy solids, which could not be readily crystallised: in each case, therefore, the thoroughly dried material was subjected forthwith to thermal decomposition.

Formation and Thermal Decomposition of Quaternary Dihydroxides.—(A) *5,5,7,7-Tetramethyl-5,7-diarsonia-1,2:3,4-dibenzocycloheptadiene dihydroxide* (I; $n = 1$; X = OH). A cold solution of the dibromide (3 g.) in water (15 ml.) was shaken overnight with freshly prepared dry silver oxide [from silver nitrate (2 g.) and sodium hydroxide (1·5 g.) in water (25 ml.)]. The mixture was then heated to the b. p. and filtered hot, and the filtrate was evaporated under nitrogen at reduced pressure. The residue, heated at 150°/0·01 mm. in a nitrogen atmosphere, yielded a partly crystalline distillate of the diarsine (II) (1·2 g.), identified by treatment with excess *of methyl iodide at 100° for 2 hr., which gave the dimethiodide, m. p. 264° (from ethanol);* the latter with sodium picrate in ethanol gave the corresponding dimethopicrate, m. p. and mixed m. p. 274—275° (from water) (lit.,[1] m. p. 283—285°).

(B) *5,5,8,8-Tetramethyl-5,8-diarsonia-1,2:3,4-dibenzocyclo-octadiene dihydroxide* (I; $n = 2$; X = OH). This compound was similarly prepared from the corresponding dibromide, or by shaking an aqueous solution of the di-iodide with silver oxide for 1 hr. only. This *di-iodide monohydrate* (I; $n = 2$; X = I), prepared from the dibromide by treatment with sodium iodide in methanol and recrystallised from methanol, had m. p. 222—223° after being heated at 60°/0·1 mm. for 6 hr. (Found: C, 33·1; H, 4·3. $C_{18}H_{24}As_2I_2,H_2O$ requires C, 32·65; H, 4·0%). The dihydroxide decomposed at 160°/0·05 mm., giving a pale yellow distillate which, redistilled under nitrogen, gave 2,2′-biphenylylenebisdimethylarsine (III), b. p. 120°/0·1 mm., identified by comparison of its infrared absorption spectrum with that of an authentic specimen and by analysis, m. p., and mixed m. p. of its dimethiodide and dimethobromide. The dimethiodide with aqueous sodium picrate deposited the yellow *dimethopicrate monohydrate*, m. p. 177° (from water or ethanolic acetone) (Found: C, 42·4; H, 3·8; N, 9·7. $C_{30}H_{30}As_2N_6O_{14},H_2O$ requires C, 41·7; H, 3·85; N, 9·8%).

Heated at 260°/0·05 mm. in nitrogen, the dimethobromide regenerated the diarsine (III); proof of identity was secured by comparison of infrared absorption spectra, which also showed that the diarsine prepared in this way was free from a trace contaminant (almost certainly biphenyl) present in the original specimen. The corresponding dihydroxide (IV; X = OH), prepared from the dimethobromide and silver oxide, decomposed at 170°/0·1 mm., giving biphenyl, m. p. and mixed m. p. 66—67° (after recrystallisation from methanol), and an intractable residue containing arsenic.

(C) *5,5,9,9-Tetramethyl-5,9-diarsonia-1,2:3,4-dibenzocyclononadiene dihydroxide* (I; $n = 3$; X = OH), prepared as above from the corresponding dibromide (3 g.), decomposed at 165°/0·5 mm., giving a solid distillate (crude 1·0 g.) of biphenyl, m. p. and mixed m. p. 69° (from methanol). The residue in the flask and the volatile products condensed in a trap cooled in liquid air proved intractable.

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Vol. 1961, page 2766, line 8. *For* monomethiodide *read* monohydriodide.

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Quaternary Salts from 2,2′-Biphenylylenebisdimethylarsine (III).—(A) *2,2′-Biphenylylenebis(allyldimethylarsonium) dibromide.* The diarsine, heated with an excess of allyl bromide in a sealed tube at 100° for 10 hr., gave the *dibromide*, m. p. 194° (from ethanol–ethyl acetate) (Found: C, 43·8; H, 5·2. $C_{22}H_{30}As_2Br_2$ requires C, 43·8; H, 5·0%). The diarsine, when heated with an equimolecular quantity of allyl bromide, gave a mixture, not readily separated, and almost certainly containing the mono- and di-quaternary salts. The dibromide decomposed at 250°/0·05 mm., giving a colourless distillate of the diarsine (III), identified by conversion into the dibromodiarsinepalladium, m. p. 280° (decomp.) [lit.,[3] m. p. 270° (decomp.)] (Found: C, 31·2; H, 3·1. Calc. for $C_{16}H_{20}As_2Br_2Pd$: C, 30·55; H, 3·2%).

(B) *Ethylidenebis-(2′-dimethylarsino-2-biphenylyldimethylarsonium) dibromide* (VII; Y = As, R = >CHMe). The diarsine (2 g.) was heated with 1,1-dibromoethane (1·1 g., 1·05 mol.) in a sealed tube at 100° for 48 hr., giving the *dibromide monohydrate*, m. p. 240° [from ethanol–light petroleum (b. p. 80—100°)] (Found: C, 43·9; H, 4·9. $C_{34}H_{44}As_4Br_2,H_2O$ requires C, 43·9; H, 4·95%). With aqueous sodium picrate this gave the corresponding yellow *dipicrate monohydrate*, m. p. 134° (from water) (Found: C, 44·5; H, 3·9; N, 7·1. $C_{46}H_{48}As_4N_6O_{14},H_2O$ requires C, 45·0; H, 4·1; N, 6·9%).

(C) *2,2′-Biphenylylenebistrimethylarsonium dibromide* (IV; X = Br). 2,2′-Biphenylylenebisdimethylarsine (3 g.) was heated with 1,3-dibromo-2,2-dimethylpropane (1·8 g.) and methanol (1 ml.) in a sealed tube at 125° for 14 days. The resulting dibromide, after recrystallisation from ethanol, had m. p. 270—280° (decomp.), alone or mixed with a specimen prepared from the diarsine (III) and methyl bromide. The infrared absorption spectra were also identical. With sodium picrate it gave the dipicrate, m. p. and mixed m. p. 175° (from ethanol–acetone) (Found: C, 41·8; H, 3·6; N, 9·8. Calc. for $C_{30}H_{30}As_2N_6O_{14},H_2O$: C, 41·7; H, 3·85; N, 9·8%).

A sample of the dibromopropane was heated with methanol in a sealed tube at 125° for 14 days: some darkening occurred, but no evidence was obtained suggesting substantial reaction, and the infrared absorption spectrum of the mixture was unchanged.

(D) *5,5,10,10-Tetramethyl-5,10-diarsonia-1,2:3,4-dibenzocyclodecadiene dibromide* (I; $n = 4$; X = Br). The diarsine (4 g.) was heated with 1,4-dibromobutane (2·1 g., 0·9 mol.) in a sealed tube at 100° for 12 hr. No suitable solvent could be found for recrystallisation of the product; it was therefore purified by precipitation from its ethanolic solution by ether, which gave the hygroscopic and apparently amorphous *dibromide sesquihydrate*, m. p. 210° (decomp.) (Found: C, 39·6; H, 5·4; ionic Br, 25·6. $C_{20}H_{28}As_2Br_2,1\frac{1}{2}H_2O$ requires C, 39·7; H, 5·2; ionic Br, 26·0%). When the dibromide (5 g.) was heated at 215°/0·1 mm. in nitrogen, it decomposed, yielding a pale yellow distillate. A sample of this distillate gave an intense yellow colour with sodium iodide in acetone, indicating the presence of a bromo-arsine; the remainder was therefore treated with excess of methylmagnesium iodide in ether. Hydrolysis with aqueous ammonium chloride and distillation then gave 9-methyl-9-arsafluorene (V), b. p. 110°/0·2 mm. (1·25 g., 60%), identified by conversion into its methiodide monohydrate, m. p. and mixed m. p. 206—207° (decomp.) (lit.,[1] m. p. 206—207°), and thence into the methopicrate, m. p. and mixed m. p. 214·5—215·5° (lit.,[1] m. p. 214·5—215·5°) (from water).

(E) *5-Bromomethyl-5,7-dimethyl-7-arsa-5-arsonia-1,2:3,4-dibenzocycloheptadiene bromide* (VI). The diarsine (II) (1·26 g.) was heated with methylene dibromide (0·6 g.) and methanol (1 ml.) in a sealed tube at 100° for 72 hr. No satisfactory solvent being found for recrystallisation, the salt was purified by precipitation from its ethanolic solution by ether, giving the *bromide monohydrate*, m. p. 202—204° (Found: C, 35·7; H, 4·2. $C_{16}H_{18}As_2Br_2,H_2O$ requires C, 35·7; H, 3·8%). With ethanolic sodium picrate this gave the yellow *picrate monohydrate*, m. p. 145—146° (from water) (Found: C, 38·0; H, 2·9%; *M*, determined [6] spectrometrically, 690. $C_{22}H_{20}As_2BrN_3O_7,H_2O$ requires C, 38·4; H, 3·2%; *M*, 687).

2,2′-Biphenylylenebisdiethylarsine.—Diethyliodoarsine (12 g.) in benzene (50 ml.) was added to a solution of 2,2′-dilithiobiphenyl prepared from 2,2′-dibromobiphenyl (7 g.) and lithium foil (1·5 g.) in ether (150 ml.) under nitrogen. After boiling under reflux for 1 hr., the mixture was hydrolysed with cold air-free water, and the organic layer was separated, dried, and evaporated. Fractionation of the residue in nitrogen gave the *diarsine*, b. p. 150°/0·2 mm. (7 g., 50%) (Found: C, 57·3; H, 6·5. $C_{20}H_{28}As_2$ requires C, 57·4; H, 6·7%). Treatment of the diarsine with excess of methyl bromide either at room temperature or at 100° in a sealed tube for 4 hr. gave the *dimethobromide*, m. p. 240° [ethanol–light petroleum (b. p. 60—80°)]

[6] Cunningham, Davies, and Spring, *J.*, 1951, 2305.

(Found: C, 42·95; H, 5·6. $C_{22}H_{34}As_2Br_2$ requires C, 43·3; H, 5·6%). With ethylene dibromide (10 mol.) in a sealed tube at 100°, the diarsine gave an apparent mixture from which no quaternary salt was isolated.

Triethylvinylarsonium Bromide.—A mixture of triethylarsine and ethylene dibromide (1 mol.) was heated under nitrogen in a pressure bottle at 100° for 6 hr. The cold crystalline product, when recrystallised from ethanol, gave *2-bromoethyltriethylarsonium bromide*, m. p. 236—237° (decomp.) (Found: C, 27·5; H, 5·2. $C_8H_{19}AsBr_2$ requires C, 27·5; H, 5·5%).

An aqueous solution of this bromide was shaken with an excess of silver oxide at room temperature for 19 hr., filtered, neutralised with hydrobromic acid, and evaporated to dryness in a desiccator. The crystalline residue, when recrystallised from acetone, gave *triethylvinylarsonium bromide*, m. p. 246° (decomp.) after heating at 160°/0·1 mm. for 8 hr. (Found: C, 35·5; H, 6·95. $C_8H_{18}AsBr$ requires C, 35·7; H, 6·7%): it gave a *picrate*, yellow crystals (from water), m. p. 170° (decomp.) after drying at 100°/0·1 mm. (Found: C, 40·2; H, 4·7. $C_{14}H_{20}AsN_3O_7$ requires C, 40·3; H, 4·83%). Hofmann [7] prepared both the above arsonium bromides in solution, but isolated only the corresponding chloroplatinates, of general formula $[R_4As]_2[PtCl_6]$.

Ethylenebis-(2-biphenylyldimethylarsonium) Dibromide (XI).—A mixture of 2-biphenylyldimethylarsine (3·5 g.) and 1·25 c.c. (1·1 mol.) of ethylene dibromide was heated under nitrogen in a sealed tube at 100° for 6 hr. The cold solid product, when triturated with ether, collected and recrystallised twice from absolute ethanol, afforded the *dibromide* (XI), m. p. 280° (effervescence) after drying at 60°/0·1 mm. for 6 hr. (Found: C, 51·1; H, 4·5; Br, 22·4. $C_{30}H_{34}As_2Br_2$ requires C, 51·2; H, 4·8; Br, 22·8%). It gave a yellow *dipicrate*, m. p. 225° after crystallisation from acetic acid and drying at 90°/0·1 mm. for 6 hr. (Found: C, 49·9; H, 4·1; N, 8·5. $C_{42}H_{38}As_2N_6O_{14}$ requires C, 50·4; H, 3·8; N, 8·4%). Repetition of the experiment with the original mixture diluted with ethanol (5 c.c.) gave the same product (XI).

2-Biphenylyl-2′-bromoethyldimethylarsonium Bromide.—A mixture of 2-biphenylyldimethylarsine (1 g.), ethylene dibromide (1·25 ml.) (3·75 mol.), and methanol (1 c.c.) was heated under nitrogen in a sealed tube at 50° for 12 hr. The excess of dibromide and the methanol were then removed under reduced pressure. The residual oil, when triturated with ether, gave a hard, white powder, m. p. 122—128° after washing with ether. This salt was dissolved in a minimum of ethanol, leaving a small residue of the dibromide (XI): the extract was filtered and the bromide precipitated by the addition of ether. This process was repeated twice more to eliminate traces of the dibromide (XI). The final precipitated *bromide* had m. p. 130—132° (effervescence) after drying at 70°/0·1 mm. for 6 hr. (Found: C, 43·1; H, 4·3; Br, 36·15. $C_{16}H_{19}AsBr_2$ requires C, 43·1; H, 4·3; Br, 35·8%). It gave a yellow *picrate*, m. p. 138—140° (from water) (Found: C, 44·7; H, 3·8; N, 7·3. $C_{22}H_{21}AsBrN_3O_7$ requires C, 44·5; H, 3·5; N, 7·1%).

An aqueous solution of the bromide was shaken with an excess of freshly prepared silver oxide for 24 hr. The filtered solution was carefully neutralised with hydrobromic acid, refiltered, and evaporated in a desiccator. The residue was triturated with ether, and the insoluble residue purified by dissolution in a minimum of cold ethanol and reprecipitation with ether, the process being repeated four times. The pure, slightly hygroscopic *2-biphenylyldimethylvinylarsonium bromide* (X) had m. p. 194—196° (effervescence) after drying at 70°/0·1 mm. for 8 hr. (Found: C, 52·25; H, 5·2. $C_{16}H_{18}AsBr$ requires C, 52·6; H, 5·0%). It gave a yellow *picrate*, m. p. 129—130° (from 19 : 1 water–ethanol) (Found: C, 51·4; H, 3·9; N, 8·1. $C_{22}H_{20}AsN_3O_7$ requires C, 51·5; H, 3·9; N, 8·2%).

2,2′-Bisdimethylaminobiphenyl.—This diamine, prepared and purified as described by Shaw and Turner,[5] had m. p. 70·5° (lit.,[5] m. p. 72—73°) (yield, 76%) (Found: C, 80·4; H, 8·7; N, 11·4. Calc. for $C_{16}H_{20}N_2$: C, 80·0; H, 8·4; N, 11·6%).

When the diamine was heated with an excess of methyl iodide and a small amount of methanol in a sealed tube at 100° for 24 hr., it gave only 2′-dimethylamino-2-biphenylyltrimethylammonium iodide, m. p. 250—251° (from ethanol) (lit.,[5] m. p. 190—192°) (Found: C, 53·8; H, 5·8; N, 7·7; ionic I, 32·7%. Calc. for $C_{17}H_{23}IN_2$: C, 53·4; H, 6·1; N, 7·3; ionic I, 33·2%). The same product, m. p. 250—251°, was formed when the base was boiled under reflux with methyl iodide and nitromethane for 3 days (Found: ionic I, 33·0%).

The diamine (4 g.) was heated with methylene dibromide (3 g.) and methanol (1 ml.) in a sealed tube at 125° for 5 days. No quaternary salt was isolated from the dark red product, and the diamine, m. p. and mixed m. p. 71—72°, was recovered.

[7] Hofmann, *Phil. Trans.*, 1860, **150**, 409; *Annalen*, 1861, Suppl. I, 156, 275.

XUM

Vol. 1961, page 2768, lines 8 *—5 *. *For* it gave only 2′-dimethylamino-2-biphenylyltrimethylammonium iodide, m. p. 250—251° (from ethanol) (lit.,[6] m. p. 190—192°) (Found: C, 53·8; H, 5·8; N, 7·7; ionic I, 32·7%. Calc. for $C_{17}H_{13}IN_2$: C, 53·4; H, 6·1; N, 7·3; ionic I, 33·2%) *read* it gave only the monohydriodide, m. p. 250—251° (from ethanol) (lit.[5], m. p. 256—257°) (Found: C, 51·8; H, 5·8; N, 7·7; ionic I, 32·7%. Calc. for $C_{16}H_{21}IN_2$: C, 52·5; H, 5·7; N, 7·6; ionic I, 34·5%).

XUM

When the diamine (4 g.) was heated with ethylene dibromide (3·3 g.) and methanol (1 ml.) in a sealed tube at 100° for 48 hr., quaternisation occurred. Recrystallisation of the product from ethanol–light petroleum (b. p. 80—100°) gave *ethylenebis-(2′-dimethylamino-2-biphenylyldimethylammonium) dibromide dihydrate* (VII; Y = N, R = ·CH_2·CH_2·), m. p. 215—216° (Found: C, 56·5; H, 6·35; N, 8·1. $C_{34}H_{44}Br_2N_4.2H_2O$ requires C, 56·5; H, 6·8; N, 7·8%). With aqueous sodium picrate this gave the corresponding yellow *dipicrate*, m. p. 105° (from water) (Found: C, 56·7; H, 5·45; N, 15·0%; *M*, determined spectrometrically, 1010. $C_{46}H_{48}N_{10}O_{14}$ requires C, 57·2; H, 5·0; N, 14·5%; *M*, 965).

When the diamine in ethanol was boiled with an equimolecular quantity of potassium tetrabromopalladate dissolved in the minimum amount of water, the filtered solution on cooling deposited dark red crystals of a *palladium dibromide complex*, m. p. 191—192° (from ethanol) (Found: C, 32·95; H, 3·9; N, 4·6; Pd, 18·5%; *M*, cryoscopic in phenanthrene, 1110; in boiling methylene dichloride, 1114. $C_{32}H_{40}Br_6N_4Pd_2$ requires C, 32·7; H, 3·4; N, 4·8; Pd, 18·2%; *M*, 1174). This complex may therefore be a dinuclear complex of sexicovalent palladium; if so, it is curious that it is formed in conditions which make the oxidation $Pd^{II} \longrightarrow Pd^{III}$ or Pd^{IV} unlikely.

We are indebted to Dr. N. Sheppard for the nuclear magnetic resonance and ultraviolet spectra and to Dr. G. Jones for infrared spectra, and to the Department of Scientific and Industrial Research for a grant (to D. M. H.).

University Chemical Laboratory, Cambridge.
University College of North Staffordshire,
Keele, Staffordshire. [*Received, January 4th*, 1961.]

540. *The Orientation of Some Bromo-1-phenylpyrazoles.*

By I. L. Finar and D. B. Miller.

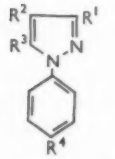
Dibromination of 3-methyl-1-phenylpyrazole in hot acetic acid gives the 4-bromo-1-*p*-bromophenyl derivative and not the 4,5-dibromo-compound as claimed by Michaelis and Behn.[1] Further bromination in nitric acid gave 4,5-dibromo-1-*p*-bromophenyl-3-methylpyrazole; this could not be prepared from 4,5-dibromo-3-methyl-1-phenylpyrazole by bromination in neutral solution but was prepared from it by a Sandmeyer reaction.

Michaelis and Behn [1] prepared 4- (I) and 5-bromo-3-methyl-1-phenylpyrazole (II) and claimed that further bromination of these two compounds produced the same dibromo-compound, 4,5-dibromo-3-methyl-1-phenylpyrazole (III). This is contrary to previous experience in this laboratory [2] where it was expected that compound (I) would form a *p*-phenyl-substituted derivative.

Michaelis and Behn's work was repeated. 3-Methyl-1-phenylpyrazole-5-carboxylic acid [3] (IX) was decarboxylated to the parent (V) and treated with bromine in cold acetic acid. The product, an oil, distilled in the range described by Michaelis for the 4-bromo-compound (I). This, with bromine in hot acetic acid, gave a solid (A) which corresponded, not with the 4,5-dibromo-compound (III), m. p. 92°, as stated by Michaelis and Behn,[1] but with the 4,*p*-dibromo-compound (IV), m. p. 98°, which was prepared as follows. The 4-bromopyrazole (I), on nitration with mixed acids at 12°, gave the *p*-nitro-compound (VI) which was also prepared by nitrating the parent (V) to the known 3-methyl-1-*p*-nitrophenylpyrazole [3,4] (VII) and brominating this in cold acetic acid. The bromo-nitro-compound (VI), on reduction with hydrazine hydrate and palladised charcoal,[5] gave the amine (VIII) which was converted into the dibromo-compound (IV) by the Sandmeyer reaction. This was identical with product (A).

[1] Michaelis and Behn, *Ber.*, 1900, **33**, 2595.
[2] Brain and Finar, *J.*, 1958, 2435.
[3] Finar and Hurlock, *J.*, 1958, 3259.
[4] Knorr, *Annalen*, 1894, **279**, 221.
[5] Dewar and Mole, *J.*, 1956, 2556.

4,5-Dibromo-1-phenylpyrazole (III), the only possible product if the second bromine atom enters the pyrazole nucleus, was prepared by means of the Borodine–Hunsdiecker reaction ($R{\cdot}CO_2Ag + Br_2 \longrightarrow RBr + AgBr + CO_2$). 3-Methyl-1-phenylpyrazole-5-carboxylic acid [3] (IX) was converted into its 4-bromo-derivative [6] (X), and the silver salt



	R^1	R^2	R^3	R^4		R^1	R^2	R^3	R^4		R^1	R^2	R^3	R^4
(I)	Me	Br	H	H	(VII)	Me	H	H	NO_2	(XIII)	Me	Br	CO_2H	H
(II)	Me	H	Br	H	(VIII)	Me	Br	H	NH_2	(XIV)	CO_2H	Br	Me	H
(III)	Me	Br	Br	H	(IX)	Me	H	CO_2H	H	(XV)	Me	Br	CO_2H	Br
(IV)	Me	Br	H	Br	(X)	Me	Br	CO_2H	H	(XVI)	Me	H	Br	NO_2
(V)	Me	H	H	H	(XI)	Me	Br	CO_2Ag	H	(XVII)	Me	Br	Br	NO_2
(VI)	Me	Br	H	NO_2	(XII)	Me	Br	Br	Br	(XVIII)	Me	Br	Br	NH_2

(XI) of this gave two products when treated with bromine in chloroform solution: the required 4,5-dibromopyrazole (III) and a more highly substituted neutral compound suspected of being a tribromo-compound [7] (XII) (cf. Brain and Finar [2]). The identity of compound (III) was established by its preparation by the Michaelis method [1] through the 5-monobromo-compound (II) (cf. Stoermer and Martinsen [8]), thereby confirming that bromination of 3-methyl-1-phenylpyrazole gives substitution initially in the 4-position of the pyrazole nucleus followed by substitution in the *para*-position of the benzene nucleus.

Musante and Berretti [6] have brominated 3-methyl-1-phenylpyrazole-5-carboxylic acid in cold acetic acid to a monobromo-acid which, although unidentified, was proved not to be 1-*p*-bromophenyl-3-methylpyrazole-5-carboxylic acid. We have repeated this and attempted to dibrominate the acid in hot acetic acid but without success. Decarboxylation of this bromo-acid gave an oil which, when brominated in hot acetic acid gave 4-bromo-1-*p*-bromophenylpyrazole (IV). Musante and Berretti's unidentified bromo-acid must therefore have been the 4-bromo-acid (X). Attempts to brominate the 4-bromo-3-acid (XIV) further also failed. It appears that a 5-bromo- or 3- or 5-carboxyl group inhibits normal dibromination in neutral solution. However, on addition of bromine to an aqueous solution of the sodium salt of the 5-acid (IX) or (X), a dibromo-acid is obtained. Decarboxylation of this gives the dibromo-compound (IV). The tribromo-derivative (XII) was also formed and is moreover obtained on addition of bromine to the sodium salt of the dibromo-acid (XV) (cf. Finar and Walter [9]).

The 4,5-dibromopyrazole (III) could not be further brominated in neutral solution. It was, however, nitrated in sulphuric acid, giving the *p*-nitro-derivative (XVII). The dibromo-compound (IV) similarly could not be further brominated in neutral solution. But in 8N-nitric acid bromination proceeded readily at room temperature to form the tribromopyrazole (XII). This was synthesised by means of the Sandmeyer reaction. The 5-bromopyrazole (II) gave the known *p*-nitrophenyl compound [1] (XVI). Bromination of this gave the 4-bromo-derivative (XVII) which was also prepared from the 4,5-dibromopyrazole (III) by nitration. Reduction of this with hydrazine hydrate and palladised charcoal [5] gave the amine (XVIII) and thence by the Sandmeyer reaction the tribromopyrazole (XII).

Experimental

4-Bromo-3-methyl-1-p-nitrophenylpyrazole.—(*a*) A mixture of sulphuric acid (35 c.c.; *d* 1·84) and nitric acid (35 c.c.; *d* 1·42) was added dropwise to 4-bromo-3-methyl-1-phenylpyrazole [1] (9·44 g., 0·04 mole) in sulphuric acid (45 c.c.; *d* 1·84) at 75° during 0·5 hr., with stirring. The solution was kept at 12° for 0·5 hr., then poured on ice. The pale yellow solid was washed and dried (10·56 g., 93%; m. p. 192—195°). On repeated recrystallisation from acetone, it gave *4-bromo-3-methyl-1-p-nitrophenylpyrazole* as pale yellow needles, m. p. 200—201° (Found:

[6] Musante and Berretti, *Gazzetta*, 1949, **79**, 668.
[7] Michaelis and Schwabe, *Ber.*, 1900, **33**, 2612.
[8] Stoermer and Martinsen, *Annalen*, 1907, **352**, 322.
[9] Finar and Walter, *J.*, 1960, 1588.

XUM

C, 42·3; H, 2·7; Br, 28·55; N, 14·6. $C_{10}H_8BrN_3O_2$ requires C, 42·6; H, 2·9; Br, 28·3; N, 14·9%).

(*b*) A mixture of bromine (1·6 g., 0·01 mole) in acetic acid (5 c.c.) was added dropwise to 3-methyl-1-*p*-nitrophenylpyrazole [4] (2·03 g., 0·01 mole) in acetic acid (50 c.c.). After 1 hr. at room temperature the needles deposited were collected, washed, and dried. The mother-liquor, when poured into water, gave more solid which was collected and dried (total 2·4 g., 85·7%; m. p. 193—194°). Recrystallisation from acetone gave 4-bromo-3-methyl-1-*p*-nitrophenylpyrazole, m. p. and mixed m. p. 199—200°.

1-p-*Aminophenyl*-4-*bromo*-3-*methylpyrazole*.—4-Bromo-3-methyl-1-*p*-nitrophenylpyrazole was refluxed with ethanol (250 c.c.), 60% hydrazine hydrate (4 c.c.), and 5% palladised charcoal [5] (0·40 g.) for 1 hr. The catalyst was filtered off, and the filtrate evaporated to small bulk, diluted with water, and set aside. Yellow plates of 1-*p*-aminophenyl-4-bromo-3-methylpyrazole separated (2·4 g., 72%), having m. p. 85—88°, raised to 86—88° on recrystallisation from methanol–water. Since the amino-compound was unstable the *acetyl derivative*, m. p. 220·5—221·5°, was analysed (Found: C, 48·7; H, 3·9; Br, 26·9; N, 14·0. $C_{12}H_{12}BrN_3O$ requires C, 49·0; H, 4·1; Br, 27·2; N, 14·3%).

4-*Bromo*-1-p-*bromophenyl*-3-*methylpyrazole*.[7]—1-*p*-Aminophenyl-4-bromo-3-methylpyrazole (5·06 g., 0·02 mole) was dissolved in 70% w/w sulphuric acid (120 c.c.) and diazotised at 5° with sodium nitrite (1·9 g., 40% excess) in sulphuric acid (6·5 c.c.; *d* 1·84). The diazonium sulphate solution was added dropwise during 20 min. to a boiling solution of cuprous bromide (7·7 g.), prepared by heating a mixture of copper sulphate pentahydrate (3·2 g.), copper turnings (1 g.), sulphuric acid (0·82 c.c.; *d* 1·84) and water (50 c.c.) for 4 hr., and adding sodium hydrogen sulphite until the solution was yellow. Steam-distillation removed solid (3 g., 48%) that on recrystallisation from methanol gave 4-bromo-1-*p*-bromophenyl-3-methylpyrazole as pale yellow needles, m. p. 97—98°, undepressed on admixture with the product of bromination of 4-bromo-3-methyl-1-phenylpyrazole in hot acetic acid (Michaelis and Schwabe [7] give m. p. 98°).

4-*Bromo*-3-*methyl*-1-*phenylpyrazole*-5-*carboxylic Acid*.[6]—3-Methyl-1-phenylpyrazole-5-carboxylic acid was brominated as described by Musante and Berretti [6] to give a monobromo-acid (m. p. 179—180°) as shown by their analysis, but unidentified by them. This bromo-acid (4 g.) was decarboxylated at 185—190°. The product, dissolved in ether, washed with 2N-sodium carbonate, dried (Na_2SO_4), and recovered, was an oil (2 g.). It was treated in chloroform with bromine and kept on a steam-bath for 1 hr., then giving a solid, which on recrystallisation from aqueous ethanol gave 4-bromo-1-*p*-bromophenyl-3-methylpyrazole. Since 1-*p*-bromophenyl-3-methylpyrazole [7] is a solid, m. p. 94°, the initial bromine atom must be in position 4 of the pyrazole nucleus.

4,5-*Dibromo*-3-*methyl*-1-*phenylpyrazole*.[1]—(*a*) Silver 4-bromo-3-methyl-1-phenylpyrazole-5-carboxylate (12·1 g., 0·03 mole) was prepared by precipitation from a neutral solution of the ammonium salt of the above acid by the addition of silver nitrate solution. It was stirred in boiling carbon tetrachloride (30 c.c.) and bromine (1·66 c.c., 0·03 mole) in carbon tetrachloride (20 c.c.) was added during 20 min. After a further 0·5 hour's refluxing, the silver bromide formed was filtered off. The carbon tetrachloride was evaporated and the residual dark oil (7·1 g.) was dissolved in ether and washed with alkali (3 × 20 c.c.), to extract unchanged acid (2·0 g.). The ether was evaporated and a portion of the residual oil (2 g.) in chloroform was passed down an alumina column and eluted with light petroleum (b. p. 40—60°) to give a white solid (1·3 g.). On rechromatography as above, 4,5-dibromo-3-methyl-1-phenylpyrazole (0·5 g., 44%), m. p. 90—91° (Michaelis and Behn [1] give m. p. 92°), was separated from a small quantity of 4,5-dibromo-3-methyl-1-*p*-bromophenylpyrazole.[7]

(*b*) This product was also prepared by the method of Michaelis and Behn,[1] with m. p. 90—92° (Michaelis and Behn give m. p. 92°), undepressed on admixture with the specimen from reaction (*a*) but depressed on admixture with the product of direct bromination of 4-bromo-3-methyl-1-phenylpyrazole.

4-*Bromo*-1-p-*bromophenyl*-3-*methylpyrazole*-5-*carboxylic Acid*.—To a stirred solution of 4-bromo-3-methyl-1-phenylpyrazole-5-carboxylic acid (6·57 g., 0·022 mole) in 0·0967N-sodium hydroxide (250 c.c.) was added bromine (3·9 g., 0·024 mole) during 15 min. Stirring was continued for 2 hr. until the solution had a straw colour. The precipitate was dissolved in ether and extracted with alkali and the alkaline extract acidified to give 4-bromo-1-*p*-bromophenyl-3-methylpyrazole-5-carboxylic acid (5·5 g., 62%), m. p. 237° on recrystallisation (Found: C, 36·6;

XUM

H, 2·5; N, 8·0. Calc. for $C_{11}H_8Br_2N_2O_2$: C, 36·7; H, 2·2; N, 7·8%). The ether extract was washed, dried (Na_2SO_4), and evaporated to give a green oil (1·75 g.). Chromatography of this in chloroform on alumina with light petroleum (b. p. 40—60°) as eluent gave a small quantity of white needles, m. p. 140—143°, which on recrystallisation from ethanol gave 4,5-dibromo-1-*p*-bromophenyl-3-methylpyrazole, m. p. 147—148° (Michaelis and Schwabe [7] give m. p. 150°).

Orientation of the Dibromo-3-methyl-1-phenylpyrazole-5-carboxylic Acid.—This dibromo-acid was decarboxylated at 240—250° for 1 hr. The product was dissolved in ether, washed with alkali, dried (Na_2SO_4), and recovered to give a solid which, on recrystallisation, gave pale yellow needles of the 4-bromo-1-*p*-bromophenylpyrazole, m. p. 97—98° undepressed on admixture with specimens previously prepared.

4,5-*Dibromo*-1-p-*bromophenyl*-3-*methylpyrazole*.[7]—(*a*) To a stirred solution of the above dibromo-acid (2·0 g., 0·0055 mole) in 0·0967N-sodium hydroxide (57·00 c.c.) was added bromine (0·9 g., 0·0056 mole) during 15 min. After 72 hr. the mixture was extracted with ether which when washed, dried (Na_2SO_4), and evaporated gave a dark green oil (1·5 g., 68%). This, on chromatography in chloroform on alumina and elution with light petroleum (b. p. 40—60°) gave 4,5-dibromo-1-*p*-bromophenyl-3-methylpyrazole,[7] m. p. 147·5—149° undepressed on admixture with the specimen prepared as above.

(*b*) To 4-bromo-1-*p*-bromophenyl-3-methylpyrazole [1] (1·58 g., 0·005 mole) in 8N-nitric acid acid (40 c.c.) was added bromine (0·8 g., 0·005 mole) during 5 min. The mixture was shaken until a dark brown sticky solid was formed. The product was washed and recrystallised from ethanol to give off-white needles of 4,5-dibromo-1-*p*-bromophenyl-3-methylpyrazole (1·63 g., 82%), m. p. 146—148°. Further recrystallisation from ethanol gave pure white needles, m. p. 147—148° undepressed on admixture with the above specimen.

4,5-*Dibromo*-3-*methyl*-1-p-*nitrophenylpyrazole*.—(*a*) Bromine (0·4 g., 0·0025 mole) in acetic acid (20 c.c.) was added during 10 min. to a solution of 5-bromo-3-methyl-1-*p*-nitrophenylpyrazole [1] (0·65 g., 0·0025 mole) in acetic acid (5 c.c.). The solution was kept at room temperature for 1 hr., then poured into an excess of water. The yellow solid was washed and dried (0·8 g., 88·9%). Recrystallisation (charcoal) from ethanol gave *4,5-dibromo-3-methyl-1-p-nitrophenylpyrazole*, m. p. 162·5—163° (Found: N, 11·3. $C_{10}H_7Br_2N_3O_2$ requires N, 11·6%).

(*b*) A mixture of sulphuric acid (10 c.c.; *d* 1·84) and nitric acid (10 c.c.; *d* 1·42) was added dropwise with stirring during 0·5 hr. to a cooled solution of 4,5-dibromo-3-methyl-1-phenylpyrazole [1] (4 g., 0·0013 mole) in sulphuric acid (10 c.c.; *d* 1·84). The temperature was kept at $\geqslant 5°$ during the addition and then at 12° for 1 hr., and finally the solution was poured on ice. The precipitate was collected, washed, and dried (4·45 g., 97·6%), m. p. 157—159°. Recrystallisation (charcoal) from ethanol gave white needles, m. p. 162·5—163°, undepressed on admixture with the specimen from (*a*).

1-p-*Aminophenyl*-4,5-*dibromo*-3-*methylpyrazole*.—4,5-Dibromo-3-methyl-1-*p*-nitrophenylpyrazole (4·0 g., 0·011 mole) was refluxed with ethanol (50 c.c.), 60% hydrazine hydrate (4·1 c.c.), and 5% palladised charcoal [8] (0·41 g.) for 1 hr. The catalyst was filtered off; the filtrate, when evaporated to small bulk, diluted, and set aside, deposited a solid (3·2 g., 87·2%). Warming this with 2N-hydrochloric acid and cooling afforded needles of 1-p-*aminophenyl*-4,5-*dibromo*-3-*methylpyrazole hydrochloride*, m. p. 262—263° (decomp.) (Found: C, 32·9; H, 3·0. $C_{10}H_{10}Br_2ClN_3$ requires C, 32·7; H, 2·7%).

4,5-*Dibromo*-1-p-*bromophenyl*-3-*methylpyrazole*.—To a cooled solution of 1-*p*-aminophenyl-4,5-dibromo-3-methylpyrazole (2·2 g., 0·0066 mole) in sulphuric acid (1·5 c.c.; *d* 1·84) and water (10 c.c.) was added sodium nitrite (0·8 g.) in water (10 c.c.). A cuprous bromide solution was prepared by refluxing a mixture of copper sulphate pentahydrate (0·63 g.), copper turnings (0·2 g.), sodium bromide (1·54 g.), water (10 c.c.), and sulphuric acid (0·16 c.c.; *d* 1·84) for 4 hr. The reduction was completed by adding a small quantity of sodium hydrogen sulphite. The cold diazonium solution was added dropwise from a cooled jacketed dropping-funnel into the boiling cuprous bromide, through which steam was passing. Material volatile in steam (0·9 g., 34·6%) afforded, on recrystallisation from ethanol, 1-*p*-bromophenyl-4,5-dibromo-3-methylpyrazole, m. p. 144·5—146° undepressed on admixture with specimens previously obtained.

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541. *The Synthesis of Some New Phenols.*

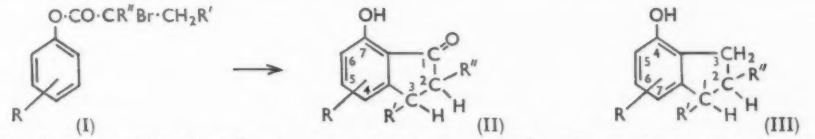
By R. E. Dean, A. Midgley, E. N. White, and D. McNeil.

2-Ethyl-3-methyl- and 3-ethyl-2-methyl-phenol, 1-, 2-, 5-, 6-, and 7-methylindan-4-ol and 1- and 4-methylindan-5-ol have been prepared for the first time. An improved synthesis of 6-methylindan-5-ol is also described.

In a recent analytical investigation of a sample of coal-tar phenols, a number of constituents not hitherto reported in the literature were isolated.[1] The syntheses now described were carried out to assist in their identification.

Ethylmethylphenols are major components of the fraction of coal-tar acids boiling at 225—240°, and of the ten possible isomers only the 2-ethyl-3-methyl- and 3-ethyl-2-methyl-phenol had not previously been described. The first has now been prepared fairly simply from 2-bromo-3-methylphenol by Grignard replacement of the bromine by an ethyl radical after protection of the hydroxyl group by methylation. Hydrolysis then gave the required phenol.

The route adopted for preparation of the 3-ethyl-2-methyl isomer required 3-hydroxy-2-methylbenzoic acid as starting material. Fieser and Lothrop [2] had obtained this acid by caustic fusion of sodium 3-aminonaphthalene-1,5-disulphonate and reported their 18—27% yields as a considerable improvement over those quoted by Perkin and Baudisch [3] who used the same method. The yield has now been increased to 76% by using the acid sodium salt and carrying out the fusion in an atmosphere of nitrogen. The substituted



(I) (II) (III)

(a) R = Me (*ortho* to OH), R′ = R″ = H. (b) R = Me (*meta* to OH), R′ = R″ = H. (c) R = Me (*para* to OH), R = R′ = H. (d) R = R″ = H, R′ = Me. (e) R = R′ = H, R″ = Me.

benzoic acid was then converted into the acetophenone by passing it admixed with acetic acid over thoria, as described by Senderens [4] for production of 2-methylacetophenone from *o*-toluic acid. Clemmensen reduction of this gave 3-ethyl-2-methylphenol. By the same reactions 3-methoxy-2-methylbenzoic acid gave the corresponding anisole and thence the phenol on hydrolysis. This compound was shown to be identical with a 2,3-substituted ethylmethylphenol isolated from tar.

The fraction of tar acids boiling at 250—280° was found to consist essentially of alkylindanols, mainly the monomethyl derivatives. The predominance of this type of structure was largely unsuspected, it having been supposed that this range of tar acids would simply consist of more highly substituted homologues of phenol. Of the six possible methylindan-4-ols all except the 1- and the 2-isomer have been found and of the six methylindan-5-ols only the 2-derivative has not been identified in tar. All the methylindan-4-ols except the 3-isomer have now been prepared for the first time, in addition to 1- and 4-methylindan-5-ol. An improved synthesis of 6-methylindan-5-ol is also described.

Reduction of the corresponding 7-hydroxy-methylindan-1-ones (II) offered the most convenient means of obtaining all the methylindan-4-ols except the 3-methyl isomer. The indanones were obtained from suitably substituted phenyl α-bromo-propionates or -butyrates (I) by treatment with aluminium chloride under conditions favouring a Fries rearrangement of the acyl radical to the position *ortho* to the hydroxyl group, followed by

[1] Dean, White, and McNeil, *J. Appl. Chem.*, 1959, **9**, 629.
[2] Fieser and Lothrop, *J. Amer. Chem. Soc.*, 1936, **58**, 749.
[3] Perkin and Baudisch, *J.*, 1909, **95**, 1883.
[4] Senderens, *Compt. rend.*, 1911, **152**, 90.

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heating to bring about ring closure. 5-, 6-, and 7-Methylindan-4-ol (IIIa, b, and c) were obtained by starting from α-bromopropionyl bromide and *o*-, *m*-, and *p*-cresol respectively; reaction of phenol with α-bromobutyryl bromide and with α-bromo-α-methylpropionyl bromide, followed by treatment with aluminium chloride, yielded the 1- and the 2-isomers (IIId and e). The yields of the combined rearrangement and cyclization stage tended to be rather low, about 40%, but the final conversion of indanones into indanols by Clemmensen reduction was generally satisfactory.

The products obtained were in general the result of *ortho*-rearrangements. In one experiment with *o*-tolyl α-bromopropionate under different conditions and at a lower temperature, a small quantity of 4-methylindan-5-ol was eventually isolated; presumably this had been formed by a *para*-shift of the acyl group, giving 5-hydroxy-4-methylindan-1-one as the intermediate compound. It might have been expected that in this instance ring closure would have occurred on the less hindered side of the benzene ring to give 5-hydroxy-6-methylindan-1-one, yielding on reduction 6-methylindan-5-ol.

Two unsuccessful attempts were made to synthesize 3-methylindan-4-ol. In the first it was intended to convert 7-methoxyindan-1-one into 4-methoxy-3-methylindene by treatment with methylmagnesium iodide followed by dehydration. This on hydrogenation and hydrolysis should then have given the required indanol. Attempts to hydrogenate the crude dehydration product gave complex products in which no detectable amounts of 4-methoxy-3-methylindane could be found by infrared examination. This failure was somewhat unexpected as syntheses of substituted 1-methylindanes from the corresponding indan-1-ones by this method have been reported.[5] The second route was analogous to that successfully applied in the preparation of 1-methylindan-5-ol. It was hoped to cyclize β-*o*-methoxyphenylbutyric acid to give 4-methoxy-3-methylindan-1-one which on reduction and hydrolysis should give 3-methylindan-4-ol. The acid was obtained in quantitative yield by the reduction of 2-methoxy-β-methylcinnamic acid, prepared by a Reformatsky reaction on 2-methoxyacetophenone, but attempts at ring closure failed.

It had previously been suggested that although cyclizations can take place *meta*- to an *ortho-para*-directing group, a powerful group such as methoxyl has a definite deactivating effect.[6] Thus β-*p*-methoxyphenylpropionic acid with hydrofluoric acid is reported as giving only 3% of 6-methoxyindan-1-one, whereas the unsubstituted β-phenylpropionic acid gives 77% of indan-1-one. Although this might indicate that cyclization is difficult at a position *meta* to a methoxyl group, this would appear to depend largely on the reagent used, since use of aluminium chloride in the above reaction with β-*p*-methoxyphenylpropionic acid increases the yield to 86%. Further, as described below, in the synthesis of 1-methylindan-5-ol 29% cyclization to a position *meta* to a methoxy-group occurs in the Friedel–Crafts ring closure of β-*p*-methoxyphenylbutyric acid.

1-Methylindan-5-ol was obtained by a 5-stage sequence from 4-methoxyacetophenone. This was converted by a Reformatsky reaction into 4-methoxy-β-methylcinnamic acid which was then reduced to the corresponding butyric acid. The acid chloride of this was cyclised with aluminium chloride to 6-methoxy-3-methylindan-1-one which on Clemmensen reduction followed by demethylation gave 1-methylindan-5-ol.

6-Methylindan-5-ol has been prepared by Fieser and Lothrop[7] in an 8-step synthesis starting from *p*-tolualdehyde. A much shorter route now devised takes advantage of the production of 6-bromoindan-5-ol in good yield directly from indan-5-ol. This was converted into a methoxyindane and a methyl group introduced by a Grignard reaction. 6-Methylindan-5-ol was then obtained by hydrolysis. The yield was rather low and the crude product contained some indan-5-ol which may have arisen by loss of the methyl group during hydrolysis or incomplete replacement of all the bromine at the previous stage.

[5] Elsner and Parker, *J.*, 1957, 592.
[6] Johnson, "Organic Reactions," John Wiley and Sons, Inc., New York, 4th edn., Vol. II, pp. 120, 157.
[7] Fieser and Lothrop, *J. Amer. Chem. Soc.*, 1936, **58**, 2052.

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4-Methylindan-5-ol was prepared by a similar sequence from 4-bromoindan-5-ol. The latter had previously been made by Hunsberger *et al.*,[8] by bromination of 6-hydroxyindane-5-carboxylic acid followed by decarboxylation. Butylation of indan-5-ol proceeds exclusively in the 6-position and, as the t-butyl group can be both readily introduced and removed, this substituent was preferred to the carboxyl group for blocking the active 6-position before bromination.

Experimental

2-Bromo-3-methylanisole.—This was obtained by the action of dimethyl sulphate (6·7 g.) on an alkaline solution of 2-bromo-3-methylphenol[9] (10 g.). 2-Bromo-3-methylanisole (7·3 g., 68%) had m. p. 42° [from light petroleum (b. p. 60—80°)] (lit.,[10] 41·5—42°).

2-Ethyl-3-methylanisole.—A solution of 2-bromo-3-methylanisole (9·1 g.) in dry ether (50 ml.) was poured on to magnesium turnings (1·2 g.) during 15 min. The mixture was maintained under reflux for a further hour, then cooled and a solution of diethyl sulphate (14·0 g.) in dry ether (30 ml.) was added during 15 min. A vigorous reaction occurred with deposition of a white precipitate. After being heated for 1 hr. the mixture was cooled and poured into ice (60 g.) and 2N-hydrochloric acid (75 ml.). The product obtained by extraction with ether was dissolved in light petroleum (b. p. 60—80°) and chromatographed on alumina, to give an almost quantitative yield of crude 2-ethyl-3-methylanisole (6·9 g., n_D^{25} 1·504).

2-Ethyl-3-methylphenol.—A solution of the crude anisole (6·9 g.) in acetic acid (50 ml.), 57% hydriodic acid (6 ml.), and 60% hydrobromic acid (10 ml.) was heated under reflux for 4 hr. in an atmosphere of carbon dioxide. The bulk of the acetic acid was removed by distillation and the residue neutralised with aqueous sodium carbonate and then extracted with ether. The ethereal solution was in turn extracted with 10% sodium hydroxide solution, and the phenol recovered from the alkaline solution by acidification with hydrochloric acid and extraction with ether. The crude phenolic material (2·1 g.) was chromatographed in light petroleum (b. p. 60—80°) on silica gel. The main fraction (1·0 g., 16%) was a low-melting solid which crystallised from light petroleum (b. p. 60—80°) to give *2-ethyl-3-methylphenol* as needles, m. p. 27·5° (Found: C, 79·6; H, 9·0. $C_9H_{12}O$ requires C, 79·4; H, 8·9%); the *phenylurethane* had m. p. 162° (Found: N, 5·4. $C_{16}H_{17}NO_2$ requires N, 5·5%).

3-Hydroxy-2-methylbenzoic Acid.—Sodium hydrogen 3-aminonaphthalene-1,5-disulphonate (100 g.) was heated in an autoclave with sodium hydroxide (200 g.) in water (200 ml.) for 12 hr. at 275—280° under an initial nitrogen pressure of 40 atm. The product was dissolved in water (charcoal), the solution was filtered and acidified, and the precipitated hydroxy-methylbenzoic acid filtered off. Further quantities of the acid were recovered by extracting the mother-liquors with ether, and purified by dissolution in aqueous sodium-carbonate, washing with ether, and precipitation with acid. 3-Hydroxy-2-methylbenzoic acid crystallised from water in needles (35·5 g., 76%), m. p. 145—146° (lit.,[3] 141—142°).

3-Methoxy-2-methylbenzoic Acid.—The acid was converted into the methyl ester of the methoxy-derivative in 83% yield by treatment with dimethyl sulphate. The liquid product was hydrolysed quantitatively with 20% aqueous potassium hydroxide to 3-methoxy-2-methylbenzoic acid, m. p. 152° (from methanol) (Found: C, 64·9; H, 6·2%; equiv., 166. Calc. for $C_9H_{10}O_3$: C, 65·05; H, 6·1%; equiv., 166·2). Fieser and Lothrop [2] give m. p. 145—146°.

3-Hydroxy-2-methylacetophenone.—A solution of 3-hydroxy-2-methylbenzoic acid (10 g.) in hot acetic acid (30 ml.) was passed over a pelleted thoria catalyst (50 ml.) at 470—480° during 4 hr. After an ethereal solution of the product had been washed with aqueous sodium carbonate, the solvent was removed to give *3-hydroxy-2-methylacetophenone* (3·2 g., 32%), m. p. 121° (from ethanol) (Found: C, 71·8; H, 6·8. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7%).

3-Methoxy-2-methylacetophenone.—Similar treatment of 3-methoxy-2-methylbenzoic acid (8·35 g.) gave *3-methoxy-2-methylacetophenone* (7·1 g.) as an oil. This was purified by elution with light petroleum (b. p. 40—60°) through a column of alumina deactivated with methanol (Found: C, 73·5; H, 7·5. $C_{10}H_{12}O_2$ requires C, 73·1; H, 7·4%).

3-Ethyl-2-methylanisole.—3-Methoxy-2-methylacetophenone (1·01 g.) was heated under

[8] Hunsberger, Lednicer, Gutowsky, Bunker, and Taussig, *J. Amer. Chem. Soc.*, 1955, **77**, 2466.
[9] Huston and Petersen, *J. Amer. Chem. Soc.*, 1933, **55**, 3879.
[10] Benkeser and Buting, *J. Amer. Chem. Soc.*, 1952, **74**, 3011.

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reflux with amalgamated zinc and dilute hydrochloric acid for 10 hr. Extraction with light petroleum (b. p. 40—60°) afforded 3-ethyl-2-methylanisole (0·73 g.) as an oil. This was not purified before demethylation.

3-Ethyl-2-methylphenol.—(a) *From 3-hydroxy-2-methylacetophenone.* The acetophenone (1·48 g.) was reduced as above during 3½ hr. to give *3-ethyl-2-methylphenol* (0·52 g., 39%) as white needles, m. p. 68°.

(b) *From 3-ethyl-2-methylanisole.* (i) The crude anisole (0·73 g.) was heated under reflux with hydriodic acid (5 ml.; *d* 1·7) for 3½ hr., then diluted with water and extracted with light petroleum. The extract was washed with 10% aqueous sodium hydroxide, and the alkaline solution acidified after washing with light petroleum. 3-Ethyl-2-methylphenol (0·24 g., 36%), m. p. 67°, was recovered from the acidic solution by extraction with light petroleum.

(ii) A solution of the anisole (3·75 g.) in benzene (25 ml.) was added to one of aluminium bromide (19 g.) in the same solvent (120 ml.). After being kept overnight the mixture was heated under reflux for 14 hr., then added to water. The benzene phase was washed with water and extracted with 10% aqueous sodium hydroxide. 3-Ethyl-2-methylphenol (0·95 g., 28%) was obtained as needles, m. p. 68°, from a petroleum extract of the acidified aqueous solution.

The m. p.s of the three samples of the phenol were not depressed on admixture with each other. Recrystallization from light petroleum raised the m. p. to 71·5° (Found: C, 79·5; H, 8·9. $C_9H_{12}O$ requires C, 79·4; H, 8·9%). The phenol gave *3-ethyl-2-methylphenoxyacetic acid*, m. p. 161° (Found: C, 68·0; H, 7·1%; equiv., 186. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%; equiv., 194), and an *α-naphthylurethane*, m. p. 120° (Found: N, 4·6. $C_{20}H_{19}NO_2$ requires N, 4·6%), *4-biphenylylurethane*, m. p. 196° (Found: N, 4·3. $C_{22}H_{21}NO_2$ requires N, 4·2%), and *p-nitrobenzoate*, m. p. 181° (Found: N, 4·9. $C_{16}H_{15}NO_4$ requires N, 4·9%).

7-Hydroxymethylindan-1-ones.—The *o-*, *m-*, and *p*-tolyl esters [11] (15 g.) of α-bromopropionic acid were each treated with aluminium chloride (30 g.) at room temperature without cooling, then heated for 4 hr. at 150—160°. The mixtures were cooled and decomposed with ice and hydrochloric acid. The tarry products were steam-distilled, the indanones crystallising from the distillates. *7-Hydroxy-6-methylindan-1-one* (3·5 g., 35%), from *o*-tolyl α-bromopropionate, was collected as needles, m. p. 80—81·5° (Found: C, 73·7; H, 6·2. $C_{10}H_{10}O_2$ requires C, 74·05; H, 6·2%); it gave an intense blue colour with ferric chloride and its 2,4-*dinitrophenylhydrazone* had m. p. 301—303° (Found: N, 16·2. $C_{16}H_{14}N_4O_5$ requires N, 16·4%). *7-Hydroxy-5-methylindan-1-one* (4·0 g., 40%), from *m*-tolyl α-bromopropionate, crystallised as needles, m. p. 123·5—125° (Found: C, 73·8; H, 6·1. $C_{10}H_{10}O_2$ requires C, 74·05; H, 6·2%). 7-Hydroxy-4-methylindan-1-one (4·3 g., 43%), from *p*-tolyl α-bromopropionate, was also obtained as needles, m. p. 112·5—114° (lit.,[12] 110°).

The rearrangement of phenyl α-bromobutyrate (15 g.) was done in a slightly different manner.[13] After the treatment with aluminium chloride (35 g.) and heating for 4 hr. at 130° the solid product was decomposed and steam-distilled as before. The oil which separated from the distillate was extracted with ether and washed with aqueous sodium carbonate and water. Removal of the solvent left 7-hydroxy-3-methylindan-1-one (5·4 g., 54%) as an oil (Conover [13] gives b. p. 63°/0·07 mm., n_D^{20} 1·5635). It formed a 2,4-dinitrophenylhydrazone, m. p. 263—264° (lit.,[13] 256°).

A modification of a method described by Bruce *et al.*[14] was used for the rearrangement and cyclization of phenyl α-bromo-α-methylpropionate (25 g.). This was added dropwise to a melt of powdered aluminium chloride (55 g.) and sodium chloride (11 g.) at 140°. On completion of the addition the temperature was raised to 180° for 5 min. and the product worked up as for the 7-hydroxy-3-isomer above, to give *7-hydroxy-2-methylindan-1-one* (5·4 g., 36%) also as an oil; it was purified by washing its almost insoluble sodium salt (Found: C, 74·1; H, 6·3%).

5-Hydroxy-4-methylindan-1-one.—*o*-Tolyl α-bromopropionate (44·8 g.) was treated with aluminium chloride (44·8 g.) in carbon disulphide (50 ml.).[15] After decomposition with hydrochloric acid the product was steam-distilled and the residue washed with ether. The extract

[11] Bischoff, *Ber.*, 1892, **25**, 1308.
[12] Hayes and Thomson, *J.*, 1956, 1585.
[13] Conover, *J. Amer. Chem. Soc.*, 1953, **75**, 4017.
[14] Bruce, Sorrie, and Thomson, *J.*, 1953, 2403.
[15] Blatt, " Organic Reactions," John Wiley and Sons, Inc., New York, 4th edn., Vol. I, p. 342.

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was washed with aqueous sodium hydroxide, and the alkaline solution acidified with hydrochloric acid and extracted with light petroleum. The dried extract was chromatographed on silica, to give crude 5-hydroxy-4-methylindan-1-one (7·7 g.).

Methylindanols.—The crude indanones (5·4 g.) were heated under reflux for 3 hr. with amalgamated zinc (10 g.) and 6N-hydrochloric acid (50 ml.). The products were washed with ether, and the phenols removed with 10% sodium hydroxide solution. After acidification the phenols were recovered by ether-extraction and crystallised from light petroleum (b. p. 40—60°). The following were thus prepared.

1-*Methylindan*-4-*ol* (2·2 g., 45%), m. p. 56—57° (Found: C, 80·9; H, 8·3. $C_{10}H_{12}O$ requires C, 81·0; H, 8·2%) [4-*biphenylylurethane*, m. p. 193° (Found: N, 4·2. $C_{23}H_{21}NO_2$ requires N, 4·1%)].

2-*Methylindan*-4-*ol* (3·75 g., 76%), m. p. 48—49° (Found: C, 80·8; H, 8·3. $C_{10}H_{12}O$ requires C, 81·0; H, 8·2%) [4-*biphenylylurethane*, m. p. 153° (Found: N, 4·3. $C_{23}H_{21}NO_2$ requires N, 4·1%)].

5-*Methylindan*-4-*ol*, (4·45 g., 90%), m. p. 100° (Found: C, 80·8; H, 8·2. $C_{10}H_{12}O$ requires C, 81·0; H, 8·2%) [*phenylurethane*, m. p. 144° (Found: N, 5·3. $C_{17}H_{17}NO_2$ requires N, 5·2%); α-*naphthylurethane*, m. p. 207° (Found: N, 4·3. $C_{21}H_{19}NO_2$ requires N, 4·4%); p-*nitrobenzoate*, m. p. 182° (Found: N, 4·7. $C_{17}H_{15}NO_4$ requires N, 4·7%); 3,5-*dinitrobenzoate*, m. p. 140° (Found: N, 8·3. $C_{17}H_{14}N_2O_6$ requires N, 8·2%)].

6-*Methylindan*-4-*ol* (4·4 g., 89%), m. p. 81·5—83° (Found: C, 81·0; H, 8·3. $C_{10}H_{12}O$ requires C, 81·0; H, 8·2%) [*aryloxyacetic acid*, m. p. 159° (Found: C, 70·3; H, 6·7%; equiv., 201. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%; equiv., 206); *phenylurethane*, m. p. 136° (Found: N, 5·3. $C_{17}H_{17}NO_2$ requires N, 5·2%); α-*naphthylurethane*, m. p. 165° (Found: N, 4·4. $C_{21}H_{19}NO_2$ requires N, 4·4%); 4-*biphenylylurethane*, m. p. 158° (Found: N, 4·1. $C_{23}H_{21}NO_2$ requires N, 4·1%); p-*nitrobenzoate*, m. p. 102° (Found: N, 4·6. $C_{17}H_{15}NO_4$ requires N, 4·7%); 3,5-*dinitrobenzoate*, m. p. 135° (Found: N, 8·4. $C_{17}H_{14}N_2O_6$ requires N, 8·2%)].

7-*Methylindan*-4-*ol* (3·4 g., 69%), m. p. 85·5—87° (Found: C, 81·0; H, 8·2. $C_{10}H_{12}O$ requires C, 81·0; H, 8·2%) [*phenylurethane*, m. p. 123° (Found: N, 5·3. $C_{17}H_{17}NO_2$ requires N, 5·2%); α-*naphthylurethane*, m. p. 144° (Found: N, 4·6. $C_{21}H_{19}NO_2$ requires N, 4·4%); 3,5-*dinitrobenzoate*, m. p. 165° (Found: N, 8·0. $C_{17}H_{14}N_2O_6$ requires N, 8·2%)].

4-Methylindan-5-ol (0·92 g., 19%), m. p. 97·5—98·0° undepressed on admixture with the specimen prepared by the alternative route described below.

β-o-*Methoxyphenylbutyric Acid.*—2-Methoxy-β-methylcinnamic acid,[16] m. p. 96—97° (32·1 g.), prepared by a Reformatsky reaction between 2-methoxyacetophenone and ethyl bromoacetate, was treated in 2% aqueous sodium hydroxide (500 ml.) with 3% sodium amalgam (650 g.) during 30 min. Then the mixture was heated to, and kept at, 70° for 24 hr. The aqueous phase was decanted, acidified with hydrochloric acid, and extracted with ether. Removal of the solvent gave a quantitative yield of the *butyric acid* which on crystallization from light petroleum (b. p. 60—80°) had m. p. 48—50° (Found: C, 68·2; H, 7·2. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%).

Attempts to cyclise this acid were made by: heating the acid chloride with aluminium chloride in carbon disulphide; heating the acid with phosphorus pentoxide at 120° for 2 hr.; treating the acid with 40% hydrofluoric acid at room temperature for 24 hr.; treating the acid with anhydrous hydrogen fluoride at 0° for 1 hr. and then allowing the fluoride to evaporate during 4 hr. at room temperature; and adding the acid to a fused melt of aluminium chloride and sodium chloride at 140° and then raising the temperature to 180° for 5 min.[14] Only unchanged material was recovered from the 40% acid; the other methods yielded unidentifiable oils. Only the last product showed evidence of ring closure on infrared examination and as it resisted reduction by both the Clemmensen and the Wolff–Kischner method, it was concluded that it was not the desired product.

β-p-*Methoxyphenylbutyric Acid.*—4-Methoxy-β-methylcinnamic acid, m. p. 155—156°, prepared by a Reformatsky reaction as above, was reduced quantitatively with sodium amalgam as above. β-p-*Methoxyphenylbutyric acid* (Found: C, 68·1; H, 7·1. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%) had m. p. 60·5—61° on crystallization from light petroleum–ether.

6-*Methoxy*-3-*methylindan*-1-*one.*—A mixture of the preceding acid (12·7 g.) and thionyl chloride (12 g.) was warmed to 45°. After 15 min. all the acid had dissolved and the reaction appeared to be complete in an hour. The excess of thionyl chloride was removed under reduced

[16] Lindenbaum, *Ber.*, 1917, **50**, 1373.

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pressure at 100°, leaving the acid chloride as a pale yellow oil. To a stirred solution of this in carbon disulphide (30 ml.) at 0°, aluminium chloride (20·4 g.) was added during 30 min. and the whole was heated under reflux at 50° for 4 hr. After cooling, the mixture was shaken with ice, hydrochloric acid, and ether, and the organic phase separated and evaporated. The residue was redissolved in ether and washed with dilute aqueous sodium hydroxide and dried, and the solvent removed to give the indanone as a yellow oil (3·3 g., 29%).

5-Methoxy-1-methylindane.—The indanone (3·3 g.) was heated in acetic acid (100 ml.) for 55 hr. with zinc amalgam (14 g.) and hydrochloric acid (20 ml.). The solution was neutralised with aqueous sodium carbonate and extracted with ether which yielded a black oil (2·5 g.). When this was chromatographed on alumina, 1 : 3 benzene–light petroleum eluted the indane as a colourless oil (2·0 g., 65%).

1-Methylindan-5-ol.—The methoxy-methylindane (2·0 g.) was demethylated as described above in the preparation of 2-ethyl-3-methylphenol. *1-Methylindan-5-ol* (1·4 g., 80%) was obtained as a brown solid which gave colourless prisms (0·5 g.), m. p. 55—55·5°, on recrystallizing from light petroleum (Found: C, 81·2; H, 8·1. $C_{10}H_{12}O$ requires C, 81·0; H, 8·2%); it gave a *phenylurethane*, m. p. 114° (Found: N, 5·1. $C_{17}H_{17}NO_2$ requires N, 5·2%).

6-t-Butylindan-5-ol.—Isobutene was passed through a molten mixture of indan-5-ol (67 g.) and toluene-*p*-sulphonic acid (3 g.) until the theoretical uptake had been achieved. The cooled mixture was dissolved in ether (200 ml.) and washed with 10% aqueous sodium hydroxide (100 ml.) and with water (50 ml.). Removal of the solvent yielded *6-t-butylindan-5-ol* (70 g., 73%), m. p. 74° [from light petroleum (b. p. 40—60°)] (Found: C, 82·8; H, 9·6. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

4-Bromo-6-t-butylindan-5-ol.—Bromine (32 g.; M/5) was added during 1 hr. to a stirred solution of 6-t-butylindan-5-ol (42 g., 0·22 mole) in acetic acid (125 ml.) at 10°, and stirring continued for a further 4 hr. After 48 hr. the mixture was poured into water (200 ml.) and extracted with ether, and the extract washed with aqueous sodium carbonate and water. Removal of the solvent gave 4-bromo-6-t-butylindan-5-ol as a brown oil (55 g., 95%).

4-Bromoindan-5-ol.—The crude butyl compound (55 g.) was heated with toluene-*p*-sulphonic acid (1 g.) for 3 hr. with a stream of carbon dioxide passing through the mixture. After cooling, the mixture was dissolved in ether, washed with 10% aqueous sodium carbonate solution (20 ml.), and extracted with 10% aqueous sodium hydroxide (150 ml.). A small amount (0·7 g.) of the alkali-insoluble butyl compound remained in the ether solution. The alkaline extract, on acidification followed by ether-extraction, gave a brown solid (38·7 g.) which yielded white needles of 4-bromoindan-5-ol (12·2 g.), m. p. 71—72° (lit.,[8] 73—74°).

4-Bromo-5-methoxyindane.—This compound, m. p. 66—67°, was prepared from the indanol by the method of Hunsberger *et al.*[8] who give m. p. 66°.

5-Methoxy-4-methylindane.—A solution of the bromo-compound (11·0 g.; 0·05 mole) in ether (50 ml.) was added to magnesium turnings (1·5 g.; 0·055 g.-atom) during 1 hr. and the whole refluxed for a further 3 hr. Dimethyl sulphate (12·6 g., 0·1 mole) in ether (20 ml.) was added and the mixture refluxed for 2 hr. Ice-cold 10% ammonium chloride solution (100 ml.) was added to the cooled mixture, and the ether layer was separated. From this a brown oil was recovered which on chromatography on deactivated alumina gave 5-methoxy-4-methylindane as a colourless oil (6·7 g., 83%; n_D^{25} 1·529).

4-Methylindan-5-ol.—The methoxy-methylindane (6·5 g.) was demethylated as described for the preparation of 2-ethyl-3-methylphenol. *4-Methylindan-5-ol* (4·6 g., 77%) was obtained as needles, m. p. 98·5—99·5°, on twice recrystallizing from light petroleum (b. p. 40—60°) (Found: C, 81·1; H, 8·1. $C_{10}H_{12}O$ requires C, 81·0; H, 8·2%) [*phenylurethane*, m. p. 118° (Found: N, 5·3. $C_{17}H_{17}NO_2$ requires N, 5·2%)].

5-Methoxy-6-methylindane.—6-Bromo-5-methoxyindane (10·7 g.), m. p. 36°, prepared by the methylation of 6-bromo-5-indanol,[17] was dissolved in dry ether (30 ml.) and mixed with magnesium turnings (1·4 g.) during 1 hr. The mixture was then heated under reflux for 3 hr., then cooled, and dimethyl sulphate (11·8 g.) was added during 15 min. with stirring. The mixture was heated for 1½ hr. under reflux, left for 24 hr. and acidified with 2N-hydrochloric acid (50 ml.). It was then extracted with ether and washed with 10% sodium hydroxide solution and water, and the solvent removed, to give a brown oil (6·2 g.). This was chromatographed on silica gel to give crude 5-methoxy-6-methylindane as a colourless oil (3·8 g., 50%; n_D^{25} 1·545).

[17] Mills and Nixon, *J.*, 1930, 2510.

6-*Methylindan*-5-*ol*.—The above methoxy-methylindane (3·8 g.) was demethylated as described for 2-ethyl 3-methylphenol. The product was a pale yellow oil (2·9 g.) that was chromatographed on silica gel from which 1 : 9 benzene–light petroleum (b. p. 40—60°) eluted a white solid (0·97 g.). Recrystallization from light petroleum yielded needles of 6-methylindan-5-ol (0·44 g., 13%), m. p. 79—80·5° (Found: C, 81·1; H, 8·0. Calc. for $C_{10}H_{12}O$: C, 81·0; H, 8·2%). Fieser and Lothrop [7] give m. p. 83—84°. Further elution with 1 : 1 benzene–light petroleum gave a sticky solid (1·35 g.) which yielded indan-5-ol, m. p. and mixed m. p. 52—53°, on recrystallization from light petroleum.

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THE COAL TAR RESEARCH ASSOCIATION,
OXFORD ROAD, GOMERSAL, NR. LEEDS.

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542. *Essential Fatty Acids. Part I. Synthesis of Linoleic, γ-Linolenic, Arachidonic, and Docosa*-4,7,10,13,16-*pentaenoic Acid.*

By J. M. OSBOND, P. G. PHILPOTT, and J. C. WICKENS.

The acids named in the title have been prepared by stereospecific partial reduction of the corresponding polyacetylenic acids. The latter were prepared by the condensation of various propargyl bromides with the di-Grignard derivatives of ω-acetylenic acids. This is a new, general, and flexible approach to this type of " skipped " polyenoic acid.

THE important group of polyunsaturated fatty acids containing *cis*-ethylenic bonds separated by a methylene group (" skipped " or " methylene interrupted " unsaturation) can be classified into three main groups: those based on (1) linoleic, (2) linolenic, and (3) oleic acid. The first series have the general structure exemplified by (XVIII—XXII) and constitute the " essential fatty acid group." In addition to their nutritional importance [1] they have the property of lowering serum-cholesterol levels [2] and there is evidence [3] that the greater the unsaturation of the acid the more effective it becomes. In this connexion they may have value in the treatment of atherosclerosis. Four representatives of this group have been synthesised by a new and flexible method; they are linoleic acid (XIX); γ-linolenic (octadeca-6,9,12-trienoic) acid (XX), a rare triethenoid acid, isolated only from the seed oil of *Oenothera biennis* [4] and having importance in the biological transformation of linoleic acid into arachidonic acid; [5] arachidonic acid [6] (XXI), probably the most important animal unsaturated acid; and docosa-4,7,10,13,16-pentaenoic acid (XXII), a constituent of brain lipids.[7]

Previous syntheses of linoleic [8] and linolenic [9] (octadeca-9,12,15-trienoic) acid were not entirely satisfactory; a single-step attachment of the carboxyl group to the sensitive

[1] Deuel and Reiser, *Vitamins and Hormones*, 1955, **13**, 29.
[2] Kinsell *et al.*, in " Essential Fatty Acids," ed. Sinclair, Butterworths, London, 1958, p. 125; Bronte-Stewart, *Brit. Med. Bull.*, 1958, **14**, 243; Hegsted, Gotsis, Stare, and Worcester, *Amer. J. Nutrition*, 1959, **7**, 5.
[3] Worne and Smith, *Amer. J. Med. Sci.*, 1959, **237**, 710.
[4] Eibner, Widenmeyer, and Schild, *Chem. Umschau*, 1927, **34**, 312; Riley, *J.*, 1949, 2728; Nevenzel and Howton, *J. Org. Chem.*, 1958, **23**, 933.
[5] Mead and Howton, *J. Biol. Chem.*, 1957, **229**, 575.
[6] Mowry, Brode, and Brown, *J. Biol. Chem.*, 1942, **142**, 671, 679; Arcus and Smedley-Maclean, *Biochem. J.*, 1943, **37**, 1.
[7] Klenk and Lindlar, *Z. physiol. Chem.*, 1955, **299**, 74; Klenk and Montag, *J. Neurochem.*, 1958, **2**, 233; Herb, Witnauer, and Riemenschneider, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 505.
[8] Raphael and Sondheimer, *J.*, 1950, 2100; Gensler and Thomas, *J. Amer. Chem. Soc.*, 1951, **73**, 4601; Walborsky, David, and Howton, *ibid.*, 1951, **73**, 2590.
[9] Nigam and Weedon, *J.*, 1956, 4052.

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polyacetylenic chain is required. In a preliminary note [10] we described the condensation of various ω-acetylenic acids, through their di-Grignard complexes, with propargyl halide derivatives; shortly after this, Sarycheva and her co-workers [11] described a similar synthesis of linoleic acid by means of the appropriate ω-acetylenic ester.

In preliminary work undeca-2,5-diyn-1-ol (V) was prepared by the method of Nigam and Weedon.[9] 1-Bromo-oct-2-yne [12] (I) with the Grignard derivative of tetrahydro-2-prop-2′-ynyloxypyran [13] gave the alcohol (V) in moderate yield after acid-hydrolysis. More conveniently, and in high yield, reaction of the di-Grignard complex of propargyl alcohol and the bromide (I) in tetrahydrofuran with cuprous chloride as catalyst gave the same alcohol. Bromination with phosphorus tribromide gave 1-bromoundeca-2,5-diyne (II). This sequence was repeated twice by the second of the two methods just mentioned and the chain extended to give crystalline but unstable alcohols (VI) and (VII) and the corresponding bromides (III) and (IV). The alcohols (V, VI, and VII) were obtained in 83, 69, and 74% yield respectively, and the bromides in 77, 77, 36% yield, respectively; the low yield of the bromide (IV) being due to polymerisation. Purification of the alcohols (VI) and (VII) by crystallisation was important and led to pure bromides; these six products were examined spectroscopically and only traces of conjugated and allenic material were detected. Similarly the bromide (III) and 5-hexyn-1-ol gave eicosa-5,8,11,14-tetrayn-1-ol in 86% yield, identical with the product obtained by reduction of the acid (XVI) with lithium aluminium hydride. Complete catalytic reduction of the alcohols (V) and (VI) and of eicosa-5,8,11,14-tetrayn-1-ol gave undecyl, tetradecyl, and eicosyl alcohol in good yield. After considerable experimentation it was found that condensation of the bromides (I—IV) with the di-Grignard derivatives of various ω-acetylenic acids (VIII—XII) (see Experimental section) was effected most efficiently in tetrahydrofuran at 20° with cuprous cyanide as catalyst. Other solvents, *e.g.*, ether, benzene, and methylene chloride, other catalysts, *e.g.*, cuprous chloride and copper, and different temperatures gave poorer yields. Thus the pairs (I) + (VIII), (I) + (IX), (II) + (X), (III) + (XI), and (IV) + (XII) gave the highly crystalline pure polyacetylenic acids (XIII—XVII) in 50—75% yields. Complete catalytic reduction of each acid (XIII—XVII) gave the saturated acids in 80—95% yield, after a theoretical uptake of hydrogen, thus showing the linearity of the product. The ultraviolet absorption spectra of the acids showed

$CH_3{\cdot}[CH_2]_4{\cdot}[C{\equiv}C{\cdot}CH_2]_x{\cdot}Br$
(I) $x = 1$
(II) $x = 2$
(III) $x = 3$; m. p. 5·5—7·5°
(IV) $x = 4$; m. p. 26·5—28°

$CH_3{\cdot}[CH_2]_4{\cdot}[C{\equiv}C{\cdot}CH_2]_x{\cdot}OH$
(V) $x = 2$; m. p. 1·2—1·5°
(VI) $x = 3$; m. p. 28—30°
(VII) $x = 4$; m. p. 56—57°

$CH{\equiv}C{\cdot}CH_2{\cdot}[CH_2]_y{\cdot}CO_2H$
(VIII) $y = 7$
(IX) $y = 6$
(X) $y = 3$
(XI) $y = 2$
(XII) $y = 1$

$CH_3{\cdot}[CH_2]_4{\cdot}[C{\equiv}C{\cdot}CH_2]_x{\cdot}[CH_2]_y{\cdot}CO_2H$
(XIII) $x = 2, y = 7$; m. p. 39·5—41·5°
(XIV) $x = 2, y = 6$; m. p. 45—46°
(XV) $x = 3, y = 3$; m. p. 53—54°
(XVI) $x = 4, y = 2$; m. p. 81—82°
(XVII) $x = 5, y = 1$; m. p. 100—101·5°

$CH_3{\cdot}[CH_2]_4{\cdot}[CH{=}CH{\cdot}CH_2]_x{\cdot}[CH_2]_y{\cdot}CO_2H$
(XVIII) $x = 2, y = 7$
(XIX) $x = 2, y = 6$
(XX) $x = 3, y = 3$
(XXI) $x = 4, y = 2$
(XXII) $x = 5, y = 1$

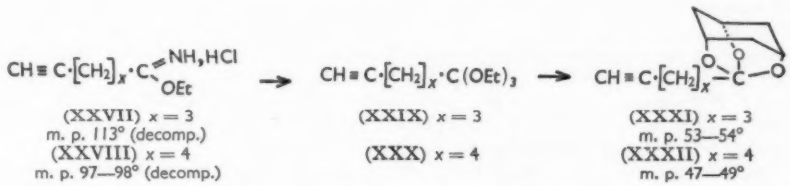
$CH_3{\cdot}[CH_2]_4{\cdot}[CHBr{\cdot}CHBr{\cdot}CH_2]_x{\cdot}[CH_2]_y{\cdot}CO_2R$
(XXIII) $x = 2, y = 6$; R = H, m. p. 114·5—116°; R = Me, m. p. 58—59°
(XXIV) $x = 3, y = 3$; R = H, m. p. 199·5—200°; R = Me, m. p. 175—177°
(XXV) $x = 4, y = 2$; R = H, m. p. 234—235°; R = Me, m. p. 228—229°

$CH{\equiv}C{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}[CH_2]_3{\cdot}CO_2H$
(XXVI) m. p. 18°

little or no conjugated material, and the infrared absorption showed the expected bands with no allene contaminant. An alternative route to the acid (XVI) was to condense

[10] Osbond and Wickens, *Chem. and Ind.*, 1959, 1288.
[11] Sarycheva, Myagkova, and Preobrazhenskii, *Zhur. obschei Khim.*, 1959, **29**, 2318.
[12] Tchao Yin Lai, *Bull. Soc. chim. France*, 1933, **53**, 682; Wotiz and Webster, *J. Org. Chem.*, 1956, **21**, 1536; Taylor and Strong, *J. Amer. Chem. Soc.*, 1950, **72**, 4263.
[13] Henbest, Jones, and Walls, *J.*, 1950, 3646.

5-hexynoic acid (XI) with propargyl bromide, giving nona-5,8-diynoic acid (XXVI) in 45% yield. The structure of this unstable acid was supported by infrared and ultraviolet absorption spectra and by reduction to nonanoic acid. The di-Grignard derivative of acid (XXVI) with 1-bromoundeca-2,5-diyne (II) under the usual conditions gave the acid (XVI) in 54% yield. The whole process could also be carried out, without isolation of the acid (XXVI), to give the product (XVI) in 55% overall yield [based on bromide (II)].



(XXVII) $x = 3$, m. p. 113° (decomp.); (XXVIII) $x = 4$, m. p. 97—98° (decomp.)

(XXIX) $x = 3$; (XXX) $x = 4$

(XXXI) $x = 3$, m. p. 53—54°; (XXXII) $x = 4$, m. p. 47—49°

Before the conditions for these condensations had been fully worked out an alternative method of protecting carboxyl groups from Grignard attack, described by Stetter and Steinacker,[14] was investigated. Treatment of 5-cyanopent-1-yne and 6-cyanohex-1-yne in ethanol with hydrogen chloride gave the two imidoyl ester hydrochlorides (XXVII) and (XXVIII), respectively, in good yield. Conversion into the ortho-esters (XXIX) and (XXX) was effected with boiling ethanol–ether or with ethanol at 20°. Transesterification with *cis*-cyclohexane-1,3,5-triol in ethanol was then rapidly achieved with boron trifluoride, or less effectively with hydrogen chloride, to give the crystalline 2,8,9-trioxa-adamantanyl derivatives (XXXI) and (XXXII) in 84% yield. The mono-Grignard derivative from these, reacting with the bromides (III) and (II), gave the protected ortho-esters of the acids (XVI) and (XV) respectively. The protecting group was then removed by acid in tetrahydrofuran–ethanol, to give in low yield the acids (XVI) and (XV) identical with samples prepared by the first method.

Partial hydrogenation of the polyacetylenic acids (XIII—XVII) was fairly extensively examined.* In all cases Lindlar's catalyst[15] was used; it was particularly suitable for obtaining almost pure polyenoic acids with the *cis*-configuration. Different solvents were employed, *e.g.*, light petroleum, benzene and ethanol. It was necessary to have conditions which allowed a rapid uptake of hydrogen at 20° to just over the theoretical value, for the hydrogenation to stop completely, and then to shake the mixture for a further period. The amount of catalyst poison (quinoline) added had to be determined for each reduction. The rate and specificity depend on the type of solvent used, the age of the catalyst (the activity of Lindlar catalyst declines with time), the purity of the substrate (old samples which are slightly oxidised are more difficult to reduce), and the temperature. The polyenoic acids (XVIII—XXII) thus obtained were converted into their methyl and ethyl esters in *ca.* 80% yield for the two steps. The purity of the esters was determined by analysis, iodine value, infrared and ultraviolet spectroscopy, alkali-isomerisation and gas-phase chromatography, the last two techniques being the most valuable and critical. Alkali-isomerisation was particularly useful in detecting small amounts of acetylenic impurity. Details are given in the Experimental section but in all cases the polyene-esters were at least 85—90% pure with little or no conjugated material and only traces of *trans*-isomer. Partial reduction of the corresponding polyacetylenic esters gave slightly more *trans*-isomer under the same conditions. Similarly, partial reduction of eicosa-5,8,11,14-tetrayn-1-ol gave eicosa-5,8,11,14-tetraen-1-ol (arachidonyl alcohol). Bromination of linoleic (XIX), γ-linolenic (XX), and arachidonic acid (XXI) and their methyl

* We acknowledge valuable advice given by Drs. H. Lindlar and S. Shaeren on this stage.

[14] Stetter and Steinacker, *Chem. Ber.*, 1952, **85**, 453; 1954, **87**, 205.
[15] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.

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esters gave the known characteristic tetra- and hexa-bromostearic and octabromoarachidic acid and their methyl esters (XXIII—XXV) with melting points in agreement with recorded values.

Experimental

The ultraviolet absorptions were measured for solution in spectroscopic ethanol. The infrared measurements were carried out on Nujol mulls or liquid films, unless otherwise stated, by Dr. A. Wagland. The method of Herb and Riemenschneider [16] was used for the alkali-isomerisation of the polyenoic esters, unless otherwise stated; some of these determinations were carried out by Dr. S. Weber. Gas-phase chromatography was carried out by Drs. A. R. Moss and J. Würsch on a column of 20% polyethylene glycol adipate (1500) on Celite; temperature 200°; argon 50 c.c./min. at 1 atmosphere; quantity 0·025—0·10 μl.; theoretical plates 3000—4000; a Pye Argon chromatograph was used as a detector.

All reactions and the general handling of all compounds containing more than one triple or double bond were conducted in a nitrogen atmosphere. Distillation residues of polyacetylenic compounds could be thermally unstable and precautions are necessary.

Undeca-2,5-diyn-1-ol (V).—(*a*) A solution of ethyl bromide (381·5 g., 3·5 moles) in dry tetrahydrofuran (300 c.c.) was added to a stirred suspension of magnesium (76·5 g., 3·15 g.-atom) under tetrahydrofuran (700 c.c.) at 0°; the internal temperature was kept at ~5°. To the Grignard reagent was added propargyl alcohol (89·6 g., 1·6 moles) in tetrahydrofuran (80 c.c.) with stirring at 3—5° during 30—45 min. and then at 20° for 2 hr. The solution was cooled to 5°, cuprous chloride (3·6 g.) was added and, after 15 min., 1-bromo-oct-2-yne [12] (18·9 g., 1·0 mole) in tetrahydrofuran dropwise during 20—30 min. The solution was heated under reflux for 24 hr., more cuprous chloride (2 g.) being added after 16 hr. The solution was added to 2N-sulphuric acid (1·5 l.) and ice, extracted with ether (3 × 400 c.c.), washed with 2N-sodium carbonate (200 c.c.) and water (2 × 200 c.c.), and dried (Na_2SO_4). The *alcohol* distilled at 80—88°/3 × 10^{-3} mm. as a colourless oil (135·8 g., 83%), n_D^{20} 1·4835, m. p. 1·2—1·5°, $\lambda_{max.}$ 267·5 mμ ($E_{1\,cm.}^{1\%}$ 9·21), $\nu_{max.}$ 3400s, 2240—2300w cm.$^{-1}$ (Found: C, 80·4; H, 10·0. $C_{11}H_{16}O$ requires C, 80·45; H, 9·8%). The *α-naphthylurethane* [from light petroleum (b. p. 80—100°)] had m. p. 98—101·5° (Found: C, 79·0; H, 6·8; N, 4·2. $C_{22}H_{23}NO_2$ requires C, 79·25; H, 6·95; N, 4·2%).

(*b*) To ethylmagnesium bromide [from magnesium (8·28 g.) and ethyl bromide (33·7 g.)] in tetrahydrofuran (250 c.c.) was added tetrahydro-2-prop-2′-ynyloxypyran [13] (47·65 g.) at 20° during 0·5 hr. The mixture was heated under reflux for 3 hr. and then treated with 1-bromo-oct-2-yne (58·5 g.) and cuprous chloride (0·9 g.) as described above. The product, after decomposition of the ammonium chloride solution, was extracted with ether and hydrolysed by toluene-*p*-sulphonic acid (2·55 g.) in boiling ethanol (300 c.c.) for 3 hr. The resulting alcohol (17·5 g., 34%) had b. p. 75—80°/9 × 10^{-5} mm., n_D^{22} 1·4821. The infrared spectrum was identical with that of sample (*a*). Complete reduction of a sample (0·5 g.) with Adams catalyst (0·1 g.) in methanol, after an uptake of hydrogen (4 mol.) gave undecan-1-ol, characterised as phenylurethane, m. p. 58—59° (lit.,[17] m. p. 62°) (Found: C, 74·2; H, 10·05; N, 4·8. Calc. for $C_{18}H_{29}NO_2$: C, 74·2; H, 10·0; N, 4·8%).

The following alcohols were prepared essentially as described in (*a*):

Tetradeca-2,5,8-triyn-1-ol (VI). 1-Bromoundeca-2,5-diyne (1 mole) and the Grignard complex of propargyl alcohol (3 moles) gave the alcohol, b. p. 135—142°/0·08 mm., n_D^{20} 1·5024, that from light petroleum (b. p. 40—60°) at −10° gave buff-coloured crystals, m. p. 28—30° (69%). Owing to the rapid autoxidation several samples gave unsatisfactory analyses (Found: C, 81·8; H, 9·0. Calc. for $C_{14}H_{18}O$: C, 83·1; H, 9·0%). The product had $\lambda_{max.}$ 270 mμ ($E_{1\,cm.}^{1\%}$ 26·0), $\nu_{max.}$ (in CCl_4) 3660m, 3500m, 2220—2300 cm.$^{-1}$. Under nitrogen at 0° the crystalline material degenerates fairly rapidly to give a red-brown polymer; it should be used within 24 hr. Hydrogenation of the alcohol (0·59 g.) over Adams catalyst (0·05 g.) in methanol (10 c.c.) gave, after a rapid uptake of hydrogen (406 c.c.; theor. 390 c.c.), tetradecan-1-ol, m. p. 38—38·5° (lit.,[17] 38°) (74%) {α-naphthylurethane [from light petroleum (b. p. 80—100°)], plates, m. p. 82° (lit.,[18] 82°)}.

[16] Herb and Riemenschneider, *J. Amer. Oil Chemists' Soc.*, 1952, **29**, 456.
[17] Ralston, "Fatty Acids and Their Derivatives," Wiley and Sons, New York, 1948.
[18] Vogel, "Practical Organic Chemistry," Longmans, Green and Co., London, 1948, p. 267.

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Heptadeca-2,5,8,11-tetrayn-1-ol (VII), prepared from 1-bromotetradeca-2,5,8-triyne (1 mole) and propargyl alcohol (6 moles) crystallised from light petroleum (b. p. 60—80°) in pale cream needles, m. p. 56—57° (74%) (Found: C, 84·45; H, 8·4. $C_{17}H_{20}O$ requires C, 84·95; H, 8·4%); it had no ultraviolet absorption and $\nu_{max.}$ (in CCl_4) 3680m, 3500m, 2220—2300w cm.$^{-1}$.

Eicosa-5,8,11,14-tetrayn-1-ol. (i) Condensation of 1-bromotetradeca-2,5,8-triyne (0·15 mole) and 5-hexyn-1-ol (0·27 mole) in tetrahydrofuran with cuprous chloride gave the tetrayne alcohol (m. p. 47·5—50°; 86%); the pure *alcohol* [from ether–light petroleum (b. p. 40—60°)] had m. p. 53·5—54·5° (Found: C, 84·9; H, 9·4. $C_{20}H_{26}O$ requires C, 85·1; H, 9·2%), $\nu_{max.}$ (in CCl_4) 3700m, 3550w, 2240—2280w, 1315s, 1050s cm.$^{-1}$.

(ii) Eicosa-5,8,11,14-tetraynoic acid (1·48 g.) in ether (100 c.c.) was added to lithium aluminium hydride (0·3 g.) in ether (100 c.c.), and the mixture boiled under reflux for 2 hr. After treatment with ethyl acetate (2 c.c.) and 2N-sulphuric acid (50 c.c.) the neutral material was obtained in the usual way and crystallised from ether–light petroleum (b. p. 40—60°) as cream-coloured plates (0·54 g.), m. p. and mixed m. p. 50·5—51·5°. A complete catalytic reduction of the tetrayne alcohol (0·7 g.) with palladised strontium carbonate in the usual way gave eicosan-1-ol, m. p. 65—65·5° (lit.,[17] 65·5°).

1-Bromoundeca-2,5-diyne (II).—To a solution of undeca-2,5-diyn-1-ol (28·97 g.) and pyridine (0·45 g.) in dry ether (125 c.c.), phosphorus tribromide (17·24 g.) was added dropwise during 0·5 hr. The solution was boiled under reflux for 3 hr., then poured on ice, and the product was extracted with ether and washed with sodium carbonate solution and water, and dried (Na_2SO_4). The bromide distilled at 86—94°/3 × 10^{-3} mm. (31 g., 77%). A portion, redistilled for analysis, had b. p. 64°/10^{-5} mm., n_D^{20} 1·5109 (Found: C, 57·6; H, 6·6; Br, 35·6. $C_{11}H_{15}Br$ requires C, 58·1; H, 6·65; Br, 35·2%), ultraviolet end absorption at 220 mμ, $\nu_{max.}$ 2280w, 2260w, trace of allene showing at 1950 cm.$^{-1}$.

1-Bromotetradeca-2,5,8-triyne (III).—Tetradeca-2,5,8-triyn-1-ol and phosphorus tribromide gave in a similar way the *bromide* (77%), b. p. 110—125°/2·5 × 10^{-3} mm., n_D^{20} 1·5245, m. p. 5·5—7·5° (Found: C, 63·0; H, 6·5; Br, 30·4. $C_{14}H_{17}Br$ requires C, 63·4; H, 6·5; Br, 30·1%).

1-Bromoheptadeca-2,5,8,11-tetrayne (IV).—In a similar way heptadeca-2,5,8,11-tetrayn-1-ol gave the corresponding bromide (36%). Before distillation the crude product was extracted with light petroleum (b. p. 40—60°) to eliminate thermally unstable polymer. The *bromide* had b. p. 160—162°/10^{-2} mm., n_D^{20} 1·5281, m. p. 26·5—28° (Found: C, 67·2; H, 6·7; Br, 26·1. $C_{17}H_{19}Br$ requires C, 67·3; H, 6·3; Br, 26·35%), $\nu_{max.}$ 2250w, 2270w cm.$^{-1}$ (C≡C).

6-Triethoxyhex-1-yne (XXIX).—To 5-cyanopent-1-yne (23·28 g., 0·25 mole) in absolute ethanol (12·66 g., 0·275 mole) at 0°, dry hydrogen chloride (10·02 g., 0·275 mole) was added. After 3 days at 5° the resulting imidoate hydrochloride (43·4 g.), m. p. 113° (decomp.), was ground with dry ether and filtered off. The hydrochloride (20·57 g.) was boiled in absolute ethanol (115 c.c.) and ether (200 c.c.) for 20 hr. Ammonium chloride (5·9 g.) was then removed, the solution concentrated, and the *orthoester* distilled; it had b. p. 104—106°/14 mm., n_D^{22} 1·4309, (15·43 g., 61%). (Found: C, 67·4; H, 10·5. $C_{12}H_{22}O_3$ requires C, 67·2; H, 10·35%), $\nu_{max.}$ 3330s (HC≡C), 2130w, 1150s cm.$^{-1}$.

7-Triethoxyhept-1-yne (XXX).—Similarly 6-cyanohex-1-yne gave the corresponding *ethyl non-8-ynimidoate hydrochloride*, m. p. 97—98° (decomp.) (80%) (Found: N, 7·3; Cl, 18·8. $C_9H_{16}ClNO$ requires N, 7·4; Cl, 18·7%). The ester hydrochloride, when kept in ethanol at 20° for 4 days, gave the *orthoester*, b. p. 103—118°/14 mm., n_D^{24} 1·4348 (50%) (Found: C, 68·85; H, 10·1. $C_{13}H_{24}O_3$ requires C, 68·4; H, 10·6%).

1-Pent-4'-ynyl-2,8,9-trioxa-adamantane (XXXI).—To a solution of 6-triethoxyhex-1-yne (11·78 g., 0·055 mole) and *cis*-cyclohexane-1,3,5-triol (6·6 g., 0·05 mole) in absolute ethanol (25 c.c.) was added boron trifluoride (45% solution, 1·5 c.c.). After 2 days at 20°, potassium carbonate (1 g.) was added and the ethanol removed. The *orthoester* crystallised from light petroleum (b. p. 40—60°) as colourless prisms (8·75 g., 84%), m. p. 53—54° (Found: C, 69·6; H, 7·8. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·75%), $\nu_{max.}$ 3300s, 2120w, 1130s cm.$^{-1}$.

1-Hex-5'-ynyl-2,8,9-trioxa-adamantane (XXXII).—In a similar way 7-triethoxyhept-1-yne gave the corresponding *orthoester* (84%), m. p. 47—49° (Found: C, 70·4; H, 8·3. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·2%).

Octadeca-9,12-diynoic Acid (XIV).—To magnesium (4·86 g., 0·2 g.-atom) under tetrahydrofuran (50 c.c.) was added ethyl bromide (23·98 g., 0·22 mole) in tetrahydrofuran (20 c.c.) during 1 hr. Reaction was initiated at 20°; the mixture was then cooled to −5° during the addition and later stirred at 20° for 3 hr. Dec-9-ynoic acid (16·8 g., 0·1 mole) in tetrahydrofuran (50 c.c.)

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was added during ¾ hr. at 0° and the whole was stirred at 20° for 2 hr. Anhydrous cuprous cyanide (0·5 g.) was added, followed after 10 min. by 1-bromo-oct-2-yne [12] (9·45 g.; 0·05 mole) in tetrahydrofuran (25 c.c.) during 15 min. at 20°. The mixture was boiled for 24 hr., poured on 2N-sulphuric acid and ice, and the product extracted with ether. The ether was extracted with 2N-ammonia, and the acidic fraction isolated in the usual way. Distillation gave fractions (i) b. p. 80—100°/0·04—0·01 mm. (6·33 g.), (ii) b. p. 100—140°/0·01 mm. (2·15 g.), and (iii) b. p. 143—154°/0·01—0·005 mm. (9·84 g.). The first two fractions were recovered decynoic acid. Fraction (iii) solidified (71%) and after crystallisation from light petroleum (b. p. 40—60°) gave the pure acid as plates (55%), m. p. 45—46° (lit.,[8] 41—43°, 42·6–44·7°) (Found: C, 77·9; H, 10·2. Calc. for $C_{18}H_{28}O_2$: C, 78·25; H, 10·2%), ultraviolet end-absorption at 220 mμ, $\nu_{max.}$ 1715s, 1755w (C=O), 2150w, 2275w cm.$^{-1}$ (C≡C), and no allene band. The *ethyl ester* prepared from the pure acid with methanolic hydrogen chloride at 20° had b. p. 182°/0·3 mm., n_D^{20} 1·4684 (Found: C, 78·45; H, 10·7. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%). The acid (0·25 g.) in methanol (20 c.c.) was hydrogenated over Adams catalyst (0·05 g.) to stearic acid, m. p. and mixed m. p. 69—70° (84%).

Nonadeca-10,13-diynoic Acid (XIII).—In a similar way 1-bromoct-2-yne and undec-10-ynoic acid gave the *diynoic acid*, b. p. 172—174°/10^{-3} mm., m. p. 39·5—41·5° (50%) (Found: C, 78·5; H, 10·35. $C_{19}H_{30}O_2$ requires C, 78·6; H, 10·4%), $\nu_{max.}$ 1715s, 1755w (C=O), 2300w, and 2125w cm.$^{-1}$ (–C≡C–) (no allene band). The *ethyl ester* had b. p. 160°/2·8 × 10^{-3} mm., n_D^{20} 1·4682 (Found: C, 78·8; H, 10·75. $C_{21}H_{34}O_2$ requires C, 79·2; H, 10·8%), $\nu_{max.}$ 1730s cm.$^{-1}$. Catalytic reduction as above gave (without purification) pure nonadecanoic acid (95%), m. p. 68—69·5° (lit.,[17] 69·5°), as plates (Found: C, 76·2; H, 12·7. Calc. for $C_{19}H_{38}O_2$: C, 76·45; H, 12·8%).

Octadeca-6,9,12-triynoic Acid (XV).—(i) Similarly 1-bromoundeca-2,5-diyne (0·04 mole) and hept-6-ynoic acid (0·09 mole) were condensed. This reaction was preferably carried out at 20° for 16 hr. It gave a 70—80% yield of the *triynoic acid*. The crude acid (very sensitive to air) was isolated by crystallisation from light petroleum (b. p. 40—60°) at −10° and formed almost colourless plates, m. p. 53·5—55° (Found: C, 79·1; H, 9·0. $C_{18}H_{24}O_2$ requires C, 79·4; H, 8·9%), $\lambda_{max.}$ 270 mμ ($E^{1\%}_{1\,cm.}$ 2·8), $\nu_{max.}$ 1700s, 2580m, 935m cm.$^{-1}$. The *methyl ester* had b. p. 140—143°/3 × 10^{-3} mm., n_D^{20} 1·4871 (Found: C, 79·2; H, 9·1. $C_{19}H_{26}O_2$ requires C, 79·7; H, 9·15%). Catalytic reduction ($6H_2$) gave pure stearic acid, m. p. and mixed m. p. 69—69·5° (85%).

(ii) To a solution of ethylmagnesium bromide (0·044 mole) in tetrahydrofuran (40 c.c.) was added 1-hex-5-ynyl-2,8,9-trioxa-adamantane (0·046 mole) in tetrahydrofuran (25 c.c.). After 1·5 hr. cuprous chloride (0·5 g.) and 1-bromoundeca-2,5-diyne (10·5 g.) were added and the mixture was boiled for 24 hr. The crude orthoester (3·9 g., 24%), b. p. 160°/5 × 10^{-3} mm., was hydrolysed in tetrahydrofuran (8 c.c.), ethanol (5 c.c.), and 2N-sulphuric acid (15 c.c.) at 80° for 1·5 hr. The acid crystallised from light petroleum (b. p. 40—60°) as prisms (0·5 g.), m. p. and mixed m. p. 52·5—53·5°.

Nona-5,8-diynoic Acid (XXVI).—Propargyl bromide (1 mole) and hex-5-ynoic acid (1 mole) condensed in tetrahydrofuran (cuprous cyanide as catalyst) at 20° (15 hr.). The product was extracted with light petroleum (b. p. 40—60°) before distillation. The pure *acid*, obtained in 45% yield (60% yield based on unrecovered hexynoic acid), had b. p. 116—117°/0·41 mm., n_D^{20} 1·4862, m. p. 18° (Found: C, 71·9; H, 6·9. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7%), ultraviolet end-absorption at 220 mμ, $\nu_{max.}$ 3320 (HC≡C), 3040s, 2680 (OH), 2150 (C≡C), 1760w, 1715, 930s cm.$^{-1}$ (C=O). The acid was sensitive to air and coloured fairly rapidly. Catalytic reduction of the acid (0·43 g.) in methanol (10 c.c.) with Adams catalyst (0·05 g.) gave rapidly (absorption 267 c.c.; theor. 286 c.c.) nonanoic acid which was converted through the acid chloride into 1-nonamide (0·31 g.), m. p. 96—98° (from ether) (lit.,[17] 98·8°).

Eicosa-5,8,11,14-tetraynoic Acid (XVI).—(i) Similarly 1-bromotetradeca-2,5,8-triyne (0·025 mole) and hex-5-ynoic acid (0·08 mole) in tetrahydrofuran either at 20° or under reflux gave the tetraynoic acid in 75—86% yield. The *acid* crystallised from light petroleum (b. p. 40—60°), isopropyl ether, or methanol as buff-coloured prisms, m. p. 81—82° (Found: C, 80·7; H, 8·15. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·2%), $\nu_{max.}$ (in CCl_4) 1750w, 1710s, 925m cm.$^{-1}$. The tetraynoic acid in 5% methanolic hydrogen chloride at 20° gave the *methyl ester* (76%), b. p. 180—185°/3 × 10^{-3} mm., n_D^{20} 1·5100, m. p. 10—12°, that darkens rapidly in air (Found: C, 80·7; H, 8·45. $C_{21}H_{26}O_2$ requires C, 81·2; H, 8·4%). The *amide*, crystallised from methanol, had m. p. 104—106·5° (Found: C, 81·7; H, 8·7. $C_{20}H_{25}NO$ requires C, 81·3; H, 8·5%), $\nu_{max.}$ 3340s,

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3180s, 1650s cm.$^{-1}$. Catalytic reduction of the acid (0·5 g.) in methanol (40 c.c.) with Adams catalyst (0·05 g.) gave arachidic acid, m. p. and mixed m. p. 75—75·5° (86%) (Found: C, 76·8; H, 12·6. Calc. for $C_{20}H_{40}O_2$: C, 76·8; H, 12·9%).

(ii) 1-Bromoundeca-2,5-diyne (1 mole) and nona-5,8-diynoic acid (2 moles) condensed in tetrahydrofuran at 20° or under reflux. The tetraynoic acid crystallised from isopropyl ether at −5° (m. p. 73—78°) and recrystallisation from methanol gave the pure acid in 54% yield, with m. p. and mixed m. p. 81·5—82°. The infrared spectra of the two acids were identical. When the whole reaction sequence from hex-5-ynoic acid ⟶ nona-5,8-diynoic acid ⟶ eicosa-5,8,11,14-tetraynoic acid was carried out, without isolation of the intermediate C_9 acid, the overall yield based on 1-bromoundeca-2,5-diyne was 55%.

(iii) In a similar way to that described above, 1-pent-4′-ynyl-2,8,9-trioxa-adamantane and 1-bromotetradeca-2,5,8-triyne gave the orthoester which without isolation was hydrolysed as before to eicosa-5,8,11,14-tetraynoic acid (from methanol), m. p. and mixed m. p. 80—82·5° (*ca.* 5%).

Docosa-4,7,10,13,16-pentaynoic Acid (XVII).—1-Bromotetradeca-2,5,8,11-tetrayne (1 mole) and pent-4-ynoic acid (3 moles) condensed in the usual way in boiling tetrahydrofuran, to give the *pentaynoic acid* in 50% yield. This separated from methanol as cream-coloured needles, m. p. 100—101·5° (soften 99°) (ultraviolet absorption nil), $\nu_{max.}$ 2650m, 1750w, 1710s, 925m cm.$^{-1}$ (Found: C, 82·2; H, 7·5. $C_{22}H_{24}O_2$ requires C, 82·5; H, 7·55%). Catalytic reduction of the acid (0·8 g.) at Adams catalyst in methanol gave ($10H_2$) docosanoic acid (80%), m. p. 80—82° (lit.,[17] 80°).

Linoleic Acid (XIX).—(i) Octadeca-9,12-diynoic acid (2·87 g.) in pure light petroleum (b. p. 60—80°; 100 c.c.) containing a 5% solution (2 c.c.) of quinoline in light petroleum was partially reduced with Lindlar catalyst [15] (0·5 g.). After a hydrogen uptake of 523 c.c. (theor. 515 c.c.) reduction virtually stopped, the catalyst was removed and the crude linoleic acid, after removal of quinoline, had m. p. −11° to −9°, n_D^{21} 1·4670, $\lambda_{max.}$ 230 ($E^{1\%}_{1\,cm.}$ 20), and showed in the infrared spectrum only a trace of *trans*-double bond at 965 cm.$^{-1}$. Purification was effected by preparation of the methyl ester (5% methanolic hydrogen chloride at 20°), b. p. 158—160°/0·4 mm., n_D^{20} 1·4604 (lit.,[17] 1·4594) (Found: C, 77·6; H, 11·6%; Iodine val., 169, 170. Calc. for $C_{19}H_{34}O_2$: C, 77·5; H, 11·6%; Iodine val., 176). The infrared spectrum indicated <1% of *trans*-isomer. The ultraviolet absorption was nil.

(ii) Ethyl octadeca-9,12-diynoate (3·72 g.) was reduced as described above. The resulting ethyl linoleate (3·02 g., 81%) had b. p. 156—158°/0·45 mm., n_D^{20} 1·4587, iodine val. 151 (theor. 164), $\lambda_{max.}$ 229 mμ ($E^{1\%}_{1\,cm.}$ 14·7), with only a trace of *trans*-isomer shown at 965 cm.$^{-1}$ in the infrared spectrum. Alkali-isomerisation [19] gave specific $\alpha = 89{\cdot}6$ at 233 mμ (theor. 92·2; 97% pure). Hydrolysis with 4% aqueous-alcoholic potassium hydroxide at 20° for 15 hr. gave linoleic acid which crystallised from light petroleum (b. p. 40—60°) at −60° and was then distilled; it had b. p. 148—152°/10^{-3} mm., n_D^{20} 1·4660, m. p. −6° to −5° (lit.,[20] n_D^{20} 1·4699, m. p. −5·2° to −5°) (Found: C, 77·2; H, 11·6%; Iodine val., 171. Calc. for $C_{18}H_{32}O_2$: C, 77·1; H, 11·5%; Iodine val., 181), $\nu_{max.}$ 3020s, 2660m, 1705s, 715m cm.$^{-1}$. The tetrabromide number was determined by Brown and Frankel's method [21] on a 0·5 g. sample: this gave a value of 80·10 (theor. 87·5; purity *ca.* 91%). Alkali-isomerisation gave specific $\alpha = 79{\cdot}75$ at 233 mμ (theor. 92·2; purity 86%). Gas-phase chromatography showed one main peak with a very small subsidiary contaminant, presumably the olefinic acid. The 9,10,12,13-tetrabromostearic acid produced by bromination in light petroleum (b. p. 30—40°) crystallised from ethylene chloride to give the pure acid, m. p. 114·5—116°. Comparison with an authentic specimen (m. p. 115—116°) by mixed m. p. and infrared spectra showed them to be identical. Synthetic tetrabromostearic acid (0·14 g.) in tetrahydrofuran was treated with ethereal diazomethane at 0° for 20 hr. The methyl ester, crystallised from light petroleum (b. p. 40—60°), had m. p. 57—58·5° (lit., [22] m. p. 56°, 63°).

Nonadeca-10,13-dienoic Acid [23] (XVIII).—Similarly, as in (ii) above, ethyl nonadeca-10,13-diynoate (3·45 g.) in light petroleum (b. p. 40—60°; 100 c.c.) and Lindlar catalyst (1·5 g.)

[19] Stillman (Report of the Spectroscopy Committee), *J. Amer. Oil Chemists' Soc.*, 1949, **26**, 399.
[20] Matthews, Brode, and Brown, *J. Amer. Chem. Soc.*, 1941, **63**, 1064.
[21] Brown and Frankel, *J. Amer. Chem. Soc.*, 1938, **60**, 54; White and Brown, *J. Amer. Oil Chemists' Soc.*, 1949, **26**, 385; 1952, **29**, 292.
[22] Haworth, *J.*, 1929, 1458; Smit, *Rev. Trav. chim.*, 1930, **49**, 543.
[23] Cf. Karrer and Koenig, *Helv. Chim. Acta*, 1943, **26**, 619; Whitcutt and Sutton, *Biochem. J.*, 1956, **63**, 469.

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(hydrogen uptake = 518 c.c.; theor. 514) gave ethyl nonadeca-10,13-dienoate (2·83 g., 81%), b. p. 116°/3 × 10^{-3} mm., n_D^{20} 1·4580 (Found: C, 78·5; H, 12·0%; Iodine val., 148. Calc. for $C_{21}H_{36}O_2$: C, 78·2; H, 11·9%; Iodine val., 157·4).

γ-Linolenic Acid (XX).—Reduction of octadeca-6,9,12-triynoic acid (13·6 g.) in ethanol (200 c.c.) containing 5% quinoline–ethanol solution (10 c.c.), with Lindlar catalyst (5 g.), was rapid at 20° (water cooling) until 3630 c.c. of hydrogen had been absorbed and then stopped (theor. 3598 c.c.). After a further hour's shaking the solution was filtered and hydrogen chloride passed in until a 5% solution had been obtained. The ethyl ester (10·7 g.) had b. p. 156°/0·2 mm., n_D^{20} 1·4678 (Found: C, 78·2; H, 11·4%; Iodine val., 237. Calc. for $C_{20}H_{36}O_2$: C, 78·35; H, 11·2%; Iodine val., 248·5) (no ultraviolet absorption), $\nu_{max.}$ 3040s, 1735s, 1650m, 970sh, 710s cm.$^{-1}$. Alkali-isomerisation based on the ethyl ester gave specific α = 71·5, 71·5, 72·6 at 268 mμ (average 87% purity, based on values given for linolenic acid [16]); no tetraene absorption was found. The methyl ester had b. p. 162°/0·5 mm., n_D^{20} 1·4680 (Found: C, 78·25; H, 11·3%; Iodine val., 269. Calc. for $C_{19}H_{32}O_2$: C, 78·0; H, 11·0%; Iodine val., 260·4), $\nu_{max.}$ 3040s, 1735s, 700s cm.$^{-1}$. Gas-phase chromatography showed the ethyl ester to be *ca.* 95% pure; only one other (small) peak appeared just before the main peak. Addition of bromine to the crude γ-linolenic acid in ether gave 6,7,9,10,12,13-hexabromostearic acid, m. p. 199·5—200°; crystallisation from ethyl methyl ketone gave the pure acid, m. p. 201—202° (lit.,[4] m. p. 196°, 200—200·8°, 203°) (Found: C, 28·6; H, 3·9; Br, 63·9. Calc. for $C_{18}H_{30}Br_6O_2$: C, 28·55; H, 4·0; Br, 63·3%). Treatment of the hexabromo-acid in tetrahydrofuran with diazomethane [4] or addition of bromine to methyl γ-linolenate gave the same methyl 6,7,9,10,12,13-hexabromostearate, m. p. 174·5—176·5° (from acetone) (lit.,[4] 170·5—171·5°) (Found: C, 29·65; H, 4·1; Br, 61·9. Calc. for $C_{19}H_{32}Br_6O_2$: C, 29·6; H, 4·2; Br, 62·1%).

Arachidonic Acid (XXI).—Reduction of eicosa-5,8,11,14-tetraynoic acid (1·48 g.) in light petroleum (b. p. 65—67°; 110 c.c.) containing 5% quinoline–light petroleum (2 c.c.) with Lindlar catalyst (0·5 g.) was rapid until 515 c.c. of hydrogen had been absorbed (theor. 480 c.c.) and then stopped. After being further shaken for 15 min. the solution was filtered, concentrated, and esterified with 5% methanolic hydrogen chloride (50 c.c.) at 20° for 20 hr. The methyl ester (80—85% yield) had b. p. 172—174°/0·3 mm., n_D^{19} 1·4802 (lit., n_D^{20} 1·4798) (Found: C, 79·0; H, 11·1%; Iodine val., 318, 312. Calc. for $C_{21}H_{34}O_2$: C, 79·2; H, 10·8%; Iodine val., 318·6), $\lambda_{max.}$ 232 mμ ($E^{1\%}_{1\,cm.}$ 19). Infrared comparison with pure natural methyl arachidonate showed them to be identical ($\nu_{max.}$ 3030s, 1735s, 965 trace, 700s, cm.$^{-1}$). Alkali-isomerisation gave specific α = 57·5 at 315 mμ (theor. 60·6; purity 95%); there was no pentaene absorption at 346 mμ. Gas-phase chromatography showed a main peak (*ca.* 93%) and two small impurities on either side. The *ethyl ester* had b. p. 176°/0·3 mm., n_D^{21} 1·4769 (Found: C, 79·3; H, 10·95%; Iodine val., 295, 294, 291. $C_{22}H_{36}O_2$ requires C, 79·5; H, 10·9%; Iodine val., 305·4), $\lambda_{max.}$ 230 mμ ($E^{1\%}_{1\,cm.}$ 20·5), $\nu_{max.}$ 3050s, 1735s, 1650w, 965 trace cm.$^{-1}$. Alkali-isomerisation gave specific α = 55·8 at 315 mμ (purity 92%). Gas-phase chromatography showed the sample to be *ca.* 90% pure with two very small contaminant peaks. The infrared absorption disclosed virtually no *trans*-isomer. Addition of bromine to arachidonic acid in ether gave the insoluble 5,6,8,9,11,12,14,15-octabromoeicosanoic acid, m. p. 234—235° (decomp.) [lit.,[24] 234—235° (decomp.)]. Similarly, methyl arachidonate gave methyl 5,6,8,9,11,12,14,15-octabromoeicosanoate, m. p. 225·5—227·5° (lit.,[25] 228·5—229·5°) (Found: C, 26·0; H, 3·7. Calc. for $C_{21}H_{34}Br_8O_2$: C, 26·3; H, 3·6%).

Docosa-4,7,10,13,16-pentaenoic Acid (XXII).—Docosa-4,7,10,13,6-pentaynoic acid (2·2 g.) was suspended in pure benzene (150 c.c.) containing 5% quinoline–benzene (3 c.c.) and hydrogenated at 20° with Lindlar's catalyst (0·5 g.). After the absorption of hydrogen had stopped (900 c.c.; theor. 850 c.c.) the solution was filtered and the crude acid converted in the usual way into the *ethyl ester* (85% yield), b. p. 147—152°/0·01 mm., n_D^{20} 1·4841 (Found: C, 80·4; H, 10·9%; Iodine val., 326. $C_{24}H_{38}O_2$ requires C, 80·4; H, 10·7%; Iodine val., 354) (no ultraviolet absorption), $\nu_{max.}$ 3040s, 1732s, 1650w, 965w, 700s cm.$^{-1}$. The *methyl ester* had b. p. 138—146°/10^{-3} mm., n_D^{20} 1·4855 (Found: C, 80·3; H, 10·9%; Iodine val., 337, 330. $C_{23}H_{36}O_2$ requires C, 80·2; H, 10·5%; Iodine val., 368·4). Alkali-isomerisation gave specific α = 45·4, 46·5, 47·43 at 346 mμ [for a natural docosapentaenoic acid [16] (structure unknown) specific α = 50·4; this indicates a purity for our sample of 96%; for an eicosapentaenoic acid [16] specific α = 87·5 at 346 mμ (purity then = 60·5%)]. Gas-phase chromatography indicated a purity of

[24] Hart and Heyl, *J. Biol. Chem.*, 1927, **72**, 399.
[25] Shinowara and Brown, *Oil and Soap*, 1938, **15**, 151.

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85—90%, there being one main peak and two small peaks, slightly greater in proportion than were obtained from the arachidonic acid samples.

Arachidonyl Alcohol.—Eicosa-5,8,11,14-tetrayn-1-ol (14·12 g.) in ethanol (200 c.c.) and quinoline (2 c.c.) was partially reduced with Lindlar catalyst (5·0 g.), with water-cooling (20°). After a hydrogen uptake of 5250 c.c. (theor. 5032 c.c.) reduction stopped and, after a further hour's shaking, the catalyst and solvent were removed. The residue in light petroleum (b. p. 40—60°) was washed with 2N-hydrochloric acid and water and dried (Na_2SO_4). The *alcohol* (12·77 g.) had b. p. 122—126°/10^{-3} mm., n_D^{20} 1·4880 (Found: C, 82·8; H, 11·95%; Iodine val., 342·1. $C_{20}H_{34}O$ requires C, 82·8; H, 11·8%; Iodine val., 350) (no ultraviolet absorption between 220 and 400 mμ), $\nu_{max.}$ 3350s, 3040s, 700s cm.$^{-1}$. Alkali-isomerisation of two different samples gave specific α = 32·8, 30·1 at 315 mμ. No pentaene absorption was detected. A standard for this compound is not known; on the basis of arachidonic acid this represents *ca.* 50% purity. However, both the iodine value and gas-phase chromatography indicate that the sample is at least 90% pure: only a trace of *trans*-isomer was detected by infrared spectroscopy.

We thank Drs. A. L. Morrison and A. Cohen for helpful discussions and Messrs. B. Gregson-Allcott, J. Howroyd, and M. Barron for skilled assistance.

Research Department, Roche Products Limited,
Welwyn Garden City, Herts.

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543. *Leucoanthocyanidins of Plants. Part III.* Leucopelargonidin from* Eucalyptus calophylla *Kino.*

By A. K. Ganguly and T. R. Seshadri.

Eucalyptus calophylla kino yields, besides aromadendrin and sakuranetin, lævorotatory leucopelargonidin (3,4,5,7,4′-pentahydroxyflavan). Reduction of aromadendrin trimethyl ether yields two isomeric flavandiols; the lower-melting racemate agrees closely in properties with the methyl ether of the natural leucopelargonidin.

The gums of Eucalyptus species, called eucalyptus kinos, have been used in medicine and a few have been chemically examined recently. Hillis [1] reported the presence, in *E. calophylla* kino of Australian origin, of aromadendrin, ellagic acid, and a small quantity of kaempferol. Satwalekar, Gupta, and Rao [2] found that *E. citriodora*, *E. robusta*, *E. globulus* and *E. pilularis* contained ellagic acid, and that *E. citriodora* yielded also aromadendrin 7-methyl ether and kaempferol 7-methyl ether. More recently work on *E. pilularis* kino [3] in this laboratory showed that is was quite rich in leucodelphinidin. Hence a further study of the kino of *E. calophylla* obtained from W. Australia has been carried out, fractional extraction being used. Light petroleum yielded a very small amount of material giving positive tests for triterpenoids. An ether extract was separated into fractions by using in succession aqueous sodium carbonate and sodium hydroxide, and the products were identified as aromadendrin and sakuranetin, respectively. Subsequent extraction of the gum with acetone yielded a phenolic substance $C_{15}H_{14}O_6$ that gave the reactions of leucoanthocyanidins and formed pelargonidin chloride when boiled with alcoholic hydrochloric acid. It was lævorotatory, formed a penta-acetate, and with

* Part II, *Tetrahedron*, 1959, **6**, 21.

[1] Hillis, *Austral. J. Sci.*, 1952, **5**, 379.
[2] Satwalekar, Gupta, and Rao, *J. Indian Inst. Sci.*, 1957, **39**, 195.
[3] Ganguly, Seshadri, and Subramanian, *Tetrahedron*, 1958, **3**, 225.

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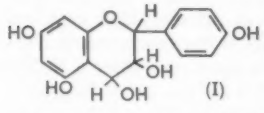
diazomethane yielded a trimethyl ether from which a diacetate was obtained. These results indicated three phenolic and two alcoholic hydroxyl groups. The methyl ether was strongly lævorotatory and its infrared spectrum had no carbonyl band. The ultraviolet spectrum was similar to those of leucocyanidin [4] and leucodelphinidin.[3]



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Permanganate oxidised the methyl ether to *p*-anisic acid. It was, therefore, concluded that the compound was leucopelargonidin (3,4,5,7,4′-pentahydroxyflavan) (I).

In efforts to prepare a synthetic leucopelargonidin derivative aromadendrin was reduced by sodium borohydride, but the product did not crystallise; after acetylation, however, a crystalline acetate was isolated; this differed in melting point from the acetate of the natural sample but agreed with it closely in the infrared spectrum. Its composition indicated that it was probably the corresponding flaven-3-yl acetate resulting from the diol by the loss of the elements of water during acetylation. In the hope of better success aromadendrin trimethyl ether was then reduced by the same reagent: two isomeric trimethoxyflavan-3,4-diols were obtained. Repeated fractional crystallisation yielded isomers of m. p. 197—200° and 150—153°. The latter agreed in melting point with the trimethyl ether obtained from natural leucopelargonidin. Janes and Morgan,[5] using different conditions, obtained only one product, melting at 161—162°. As Robertson [6] remarked, the nature of the reduction product and the proportion and ease of separation of the isomers seem to depend on the optical purity of the starting material as well as on the experimental conditions.

Though the presence of leucopelargonidin was noted earlier by qualitative methods, the isolation and description of leucopelargonidin is given here for the first time. The presence of sakuranetin in this kino is also new; it is a 7-methyl ether, in this respect similar to the 7-methyl ethers of aromadendrin and kaempferol found in *E. citriodora*.[2]

Experimental

Extraction.—Eucalyptus calophylla kino was procured through the help of the Council of Scientific and Industrial Research Organisation, Western Australia. The powdered gum (600 g.) was extracted repeatedly with low-boiling light petroleum (b. p. 40—60°): concentration of the extracts yielded a small amount of a substance which answered the Liebermann–Burchard reaction. The residual gum was extracted repeatedly with cold ether, and the ether extract was concentrated to about 800 c.c. and shaken with aqueous saturated sodium hydrogen carbonate (no extraction), 20% aqueous sodium carbonate (fraction A), and 3% aqueous sodium hydroxide (fraction B). Complete evaporation of the remaining ether solution left no residue. The gum left after the ether-extraction was subsequently extracted repeatedly with cold acetone, and the combined acetone extracts were evaporated under reduced pressure. The red sticky solid thus obtained was extracted repeatedly with ethyl acetate in the cold and these extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The concentrate was subjected to fractional precipitation by light petroleum (b. p. 40—60°) whereby coloured impurities were precipitated first and the leucoanthocyanidin (fraction C) was eventually obtained crystalline.

Fraction A (*Aromadendrin*).—When acidified with hydrochloric acid fraction A yielded a light brown solid (12 g.) that was filtered off, dried, and crystallised from methanol, yielding colourless needles, m. p. 246—247°. In alcoholic solution it gave a red colour with magnesium or zinc and hydrochloric acid. It gave a purple (changing to brown) ferric reaction. When methylated by dimethyl sulphate (3 mol.) and potassium carbonate (excess) in acetone for 10 hr. by the procedure of Goel *et al.*,[7] it gave a colourless *trimethyl ether* that crystallised from dilute methanol as rectangular tablets, m. p. 144—146°, and gave no colour with alcoholic

[4] Ganguly and Seshadri, *Tetrahedron*, 1959, **6**, 21.
[5] Janes and Morgan, *J.*, 1960, 2562.
[6] Robertson, *Canad. J. Chem.*, 1959, **37**, 1946.
[7] Goel, Narasimhachari, and Seshadri, *Proc. Indian Acad. Sci.*, 1954, **39**, *A*, 254.

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ferric chloride. With acetic anhydride and pyridine the methyl ether yielded an ***acetate***, needles (from methanol), m. p. 126—128° (Found: C, 64·2; H, 5·7. $C_{20}H_{20}O_7$ requires C, 64·5; H, 5·4%). With iodine and fused potassium acetate in acetic acid (cf. Mahesh and Seshadri [8]) the aromadendrin gave a good yield of kaempferol.

Fraction B (*Sakuranetin*).—On acidification fraction B yielded a yellow solid (5 g.) which was filtered off and dried. The compound could not be satisfactorily purified by crystallisation and hence its benzene solution was passed through a column of cellulose powder and the column washed repeatedly with benzene. The solid recovered by evaporation of the combined percolates, crystallised from dilute methanol as colourless needles, m. p. 152—153°, alone or mixed with authentic sakuranetin. Its alcoholic solution gave a wine-red colour with ferric chloride and a red colour with magnesium and hydrochloric acid. It gave no colour with zinc and hydrochloric acid. Its acetate melted at 97—98° alone or mixed with sakuranetin diacetate.

Fraction C (*Leucopelargonidin*) (I).—The leucoanthocyanidin was passed in aqueous alcohol through a long cellulose column, and the column washed repeatedly with water. The combined percolates were saturated with salt and extracted repeatedly with ethyl acetate; the extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Fractional precipitation by light petroleum then first removed impurities, and *leucopelargonidin* was obtained as colourless crystals (20 g.) (Found: C, 55·0, 54·7; H, 5·6, 5·8. $C_{15}H_{14}O_6,2H_2O$ requires C, 55·2; H, 5·5%). Its alcoholic solution was lævorotatory. It was soluble in water, alcohol, and acetone but insoluble in benzene and chloroform. The alcoholic solution gave a bluish-violet ferric reaction. When boiled with alcoholic hydrochloric acid it formed a red solution. Conversion into pelargonidin chloride was effected by the procedure described for leucodelphinidin [3] [yield 10%; R_F (circular), phenol–water lower layer at 30°, 0·9]. An ethanolic hydrochloric acid solution of the anthocyanidin chloride had $\lambda_{max.}$ 530 mμ.

Leucopelargonidin penta-acetate was prepared by acetic anhydride and pyridine in the cold; it crystallised from ethyl acetate–light petroleum as prisms, m. p. 170° (decomp.; sintering at 163°) (Found: C, 59·8; H, 5·0. $C_{25}H_{24}O_{11}$ requires C, 60·0; H, 4·8%). Its infrared spectrum had main bands at 5·66s, 6·20m, 6·66s, 7·30s, and 8·31w.

Methylation of the leucopelargonidin was by ethereal diazomethane. The colourless ***trimethyl ether*** crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as prisms, m. p. 148—150°, $[\alpha]_D$ −122·8° (Found: C, 64·8; H, 6·6. $C_{18}H_{20}O_6$ requires C, 65·0; H, 6·1%). An alcoholic solution gave no ferric reaction and with hydrochloric acid the ether gave a red colour. The infrared spectrum had main bands at 6·20s, 6·28s, 6·88s, 7·45m, 8·71s, 8·95s, 9·32s, 9·50s, 9·65s, and 10·30w. The ether with acetic anhydride and pyridine gave its *diacetate*, m. p. 182—184° [from ethyl acetate–light petroleum (b. p. 40—60°)] (Found: C, 63·7; H, 5·8. $C_{22}H_{24}O_8$ requires C, 63·4; H, 5·8%).

Potassium permanganate was added to a boiling acetone solution of the methyl ether during 6 hr. and the product worked up as described in the case of leucodelphinidin.[3] The purified acid product melted at 182—183°, alone or mixed with *p*-anisic acid.

Synthesis of Leucopelargonidin Methyl Ethers.—To a methanolic solution (50 c.c.) of aromadendrin trimethyl ether (0·1 g.) at 0° sodium borohydride (30 mg., excess) was added in one lot. After 48 hr. at room temperature (30°) the mixture was acidified with acetic acid, filtered, and evaporated almost completely under reduced pressure, and the residue was kept in the vacuum-desiccator over potassium hydroxide. The resulting colourless solid was treated with boiling water to decompose the boron complex and filtered hot. The residue was dried and crystallised fractionally from methanol; two fractions were obtained. After repeated recrystallisation the first fraction (50 mg.) formed colourless needles, m. p. 150—153° (Found: C, 64·5; H, 6·3. Calc. for $C_{18}H_{20}O_6$: C, 65·0; H, 6·1%). The second fraction (30 mg.) crystallised from methanol as colourless cubes, m. p. 197—200° (Found: C, 65·0; H, 5·9%). A mixed m. p. of each fraction with aromadendrin methyl ether was depressed. The first fraction did not depress the m. p. of the methyl ether of leucopelargonidin (natural) and its infrared spectrum had the same main bands.

Reduction of Aromadendrin.—To an ice-cold solution of aromadendrin (0·1 g.) in methanol (50 c.c.) sodium borohydride (30 mg., excess) was added in one lot. It was worked up as above and the crude product was treated with acetic anhydride and pyridine at room temperature. The colourless *acetate* crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as cubes,

[8] Mahesh and Seshadri, *Proc. Indian Acad. Sci.*, 1955, **41**, *A*, 210.

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m. p. 275° (decomp.; after sintering at 262°) [Found: C, 62·9; H, 4·9. $C_{23}H_{20}O_9$ (enol acetate) requires C, 62·7; H, 4·6%]. The infrared spectrum had main bands at 5·67s, 6·21s, 6·63s, 7·28s, and 8·30w and agreed with that of the leucoanthocyanidin acetate though the m. p. did not.

CHEMISTRY DEPARTMENT, UNIVERSITY OF DELHI,
DELHI, INDIA.

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544. *Hydrogen Bonding in Aqueous Solutions of Maleic Acid.*

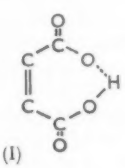
By (the late) R. E. DODD, R. E. MILLER, and W. F. K. WYNNE-JONES.

Interproton distances required to account for the observed values of the dissociation constants, K_1 and K_2, for maleic and fumaric acid are calculated on the assumption that only electrostatic and dipole interaction is significant. Agreement with reasonable dimensions of the molecules shows that the values of K_1 and K_2 for maleic acid do not require assumption of hydrogen bonding.

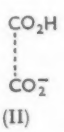
Infrared spectral evidence suggests that the acid maleate ion is, but maleic acid itself is not, internally hydrogen-bonded in approximately 1M-aqueous solution.

THE first and the second dissociation constant for maleic acid have frequently been regarded as anomalous and recently it has been thought necessary to introduce the concept of hydrogen bonding in the acid ion (I) to explain the experimental values,[1,2] and measurement of the dissociation constants in water and heavy water have been made in order to determine the relative strengths of the hydrogen and deuterium bonds.[3] Such hydrogen bonding occurs in the crystal [4] but evidence for its occurrence in solution is necessarily indirect.

The ratio of the dissociation constants of a dibasic acid was first studied quantitatively by Bjerrum [5] and later by Kirkwood and Westheimer.[6] It was shown that K_1/K_2 was always greater than four and approached this value as the separation of the carboxyl groups increased. Deviations from this value could be accounted for in terms of electrostatic interaction between the carboxylate ion and the un-ionized carboxyl groups in the structure (II). Naturally this interaction becomes greater as the two carboxyl groups approach one another.



(I)



(II)

In this paper we give the results of a calculation of electrostatic effects which show that the postulate of hydrogen bonding is not necessary for an explanation of the values of K_1 and K_2 in maleic acid. Some infrared spectral evidence is then presented which suggests that in aqueous solutions, admittedly more concentrated than those in which dissociation constants are determined, maleic acid is not internally hydrogen-bonded but that the acid maleate ion is.

[1] Hunter, *Chem. and Ind.*, 1953, **17**, 155.
[2] McDaniel and Brown, *Science*, 1953, **118**, 370.
[3] Dahlgren and Long, *J. Amer. Chem. Soc.*, 1960, **82**, 1303.
[4] Shahat, *Acta Cryst.*, 1952, **5**, 763.
[5] Bjerrum, *Z. phys. Chem.*, 1923, **106**, 219.
[6] Kirkwood and Westheimer, *J. Chem. Phys.*, 1938, **6**, 506.

Calculation

By using equations developed by Kirkwood and Westheimer it is possible to predict the separation distance of the two carboxyl groups required to produce a given value of ΔpK. These interprotonic distances (R) have been estimated for maleic and fumaric acids in both water and heavy water, the experimental values obtained by Dahlgren and Long [3] being used. The acids are considered as spherical molecules and the results are given in the Table.

Acid	Solvent	pK_1	pK_2	R	$R_{max.}$	Bjerrum's value
Maleic	H_2O	1·910	6·332	3·63	4·32	0·8
,, ...	D_2O	2·535	6·711	3·68	—	—
Fumaric	H_2O	3·095	4·602	5·12	6·74	—
,, ...	D_2O	3·557	5·025	5·16	—	—

The Table also includes the value of R calculated by application of Bjerrum's original treatment to maleic acid and the probable maximum value of R, $R_{max.}$. This was calculated by using Kirkwood and Westheimer's assumption that the protons were located 1·45 Å from the carboxyl carbon atoms on the extension of the terminal C–C bonds.[6]

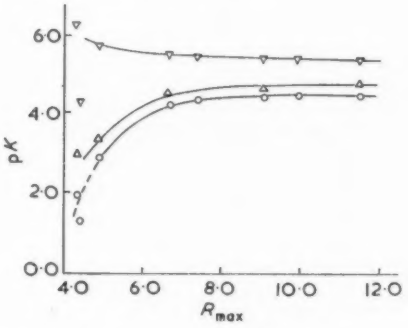


Fig. 1. *Dissociation constant as a function of* $R_{max.}$. ○ pK_1, ▽ pK_2, △ pK *of monoethyl ester. The acids shown are, in order of increasing* $R_{max.}$, *maleic, oxalic, malonic, succinic, glutaric, adipic, pimelic, and suberic.*

It can be seen that application of Bjerrum's original equation to maleic acid gives much too low a result, as is to be expected. On the other hand, the application of Kirkwood and Westheimer's equations leads to perfectly reasonable results, the difference between R and $R_{max.}$ being comparable to that found by these authors for a number of other dibasic acids. The change in ΔpK between H_2O and D_2O is seen on this interpretation as the result of only a very small increase (*ca.* 0·05 Å) in interprotonic distance. Such an increase is not unexpected.

Electrostatic interaction of the type postulated here should have very little effect on K_1 but should produce a considerable drop in K_2. On the other hand, hydrogen bonding should cause an increase in K_1 over the expected value due to the stabilisation of the acid anion if internal hydrogen bonding were more important in the acid anion than in the free acid. For the same reason a decrease in K_2 should occur. A decision as to which of the effects are operating might therefore be possible from an examination of K_1 for maleic acid. The dissociation constants for a series of acids are shown in Fig. 1 where they are plotted against the structural distance $R_{max.}$ defined above. It must be emphasised that calculation of this distance depends purely on the geometry of the molecules concerned. It can be seen that the values of both K_1 and K_2 change little at values of $R_{max.}$ greater than about 7 Å. The value of K_2 for maleic acid is low, but K_2 values for both malonic acid and succinic acid are also falling slightly as $R_{max.}$ decreases. In any case, a low value of K_2 is to be expected. K_1 for maleic acid appears to lie on a smooth curve with acids of the type $HO_2C{\cdot}[CH_2]_n{\cdot}CO_2H$ as would be expected if dipole interaction were

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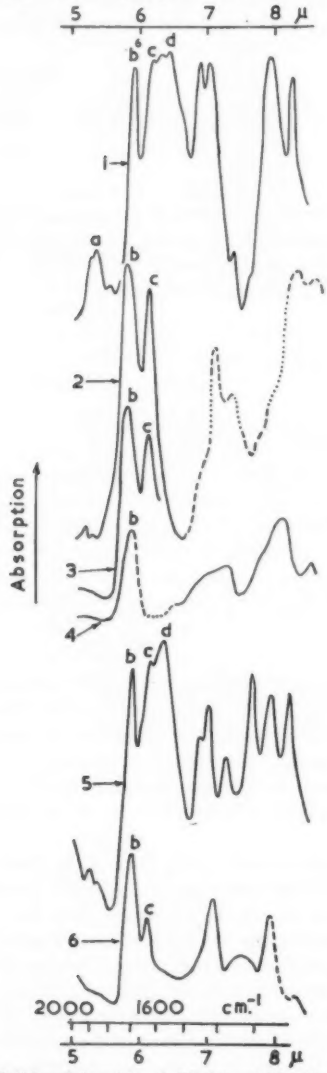
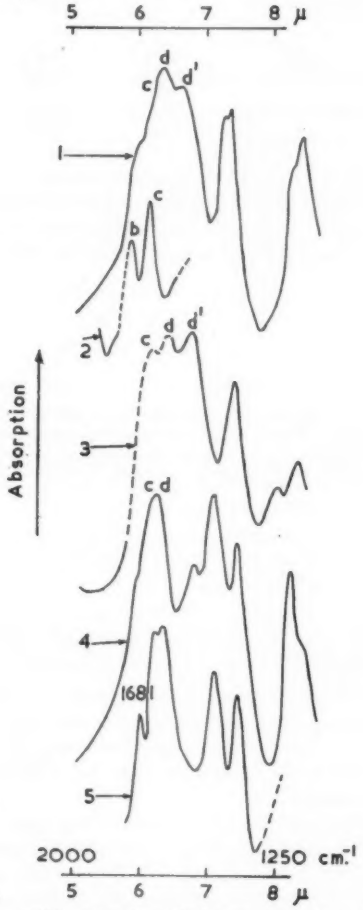
FIG. 2. *Infrared spectra of maleic acid and deuteromaleic acid, as solid and in various solvents, between 5 and 8 μ. The broken line indicates regions of solvent absorption exceeding 70% and the dotted lines indicate complete extinction by solvent.*



1, *Solid maleic acid.* 2, *Maleic acid in dioxan.* 3, *Maleic acid in methanol.* 4, *Maleic acid in water.* 5, *Solid maleic dideuteroacid.* 6, *Maleic dideuteroacid in deuterium oxide.*

FIG. 3. *Infrared spectra of potassium hydrogen maleate and potassium deuterium maleate, as solid and in various solvents, between 5 and 8 μ.*



1, *Solid potassium hydrogen maleate.* 2, *Potassium hydrogen maleate in dioxan.* 3, *Potassium hydrogen maleate in water.* 4, *Solid potassium deuterium maleate.* 5, *Potassium deuterium maleate in deuterium oxide.*

becoming more important with decreasing carboxyl separation and the C=C bond had had little effect. The acid dissociation constants of the monoesters of various dibasic acids lie on a similar curve [7] and in this case dipole interaction between ethoxycarbonyl and carboxyl groups appears to be the only explanation for the increase of K_1 as the separation distance falls.

Calculations by Westheimer and Benfey [8] suggest that hydrogen bonding is an appreciable but not dominant factor leading to a high K_1/K_2 ratio for maleic acid. They suggest that the maximum effect of hydrogen bonding would be to increase K_1/K_2 by a factor of about 28 over the statistical value. Their result rests on the assumption that an ethoxycarbonyl group has the same effect as a carboxyl group on the ionisation of an adjacent carboxyl group. This assumption may not be justified at very low separations.

We conclude that calculations based on dissociation-constant data for dibasic acids shed little light on the nature of the acid maleate ion in solution. For some of the substituted succinic acids investigated by Eberson,[9] where K_1/K_E and K_1/K_2 ratios are extremely high, it seems necessary to postulate hydrogen bonding. For maleic acid these ratios can be satisfactorily accounted for by electrostatic interaction although the calculations are of such an approximate nature that hydrogen bonding cannot be ruled out. To throw further light on this problem we have measured the infrared spectra of solutions of maleic acid and its salts in both water and heavy water.

Evidence from infrared spectra

Experimental.—The infrared absorption spectra of maleic acid, of potassium hydrogen maleate, and of sodium hydrogen fumarate, and also of the corresponding deuterated compounds,

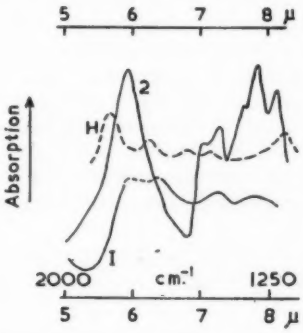


Fig. 4. *Infrared spectra of sodium hydrogen fumarate, as solid* (1) *and in aqueous solution* (2), *between* 5 *and* 8 μ. *Curve H is for the solid, as found by Hadži and Novak.*[12]

have been measured in the solid and in aqueous (or D_2O) solution. Some spectra were also measured in dioxan and in methanol. A Grubb–Parsons double-beam GS2 spectrometer was used. Particular attention was paid to the region 5—8 μ, and the spectra in that region are shown in Figs. 2, 3, and 4. Solids were mounted in potassium bromide discs (1·0—1·3 mg. in ½-in. diam. disc with about 200 mg. of potassium bromide). We are indebted to Mrs. B. S. Crawford for the preparation and infrared examination of these discs. The solutions were either 1M or saturated, and they were mounted in capillary thickness between silver chloride plates. The spectra shown are difference spectra, the solvent contribution being balanced out by careful adjustment of a similar cell in the blank beam. Exact balance at capillary thickness is only achieved by trial, and the results were confirmed by observation of difference spectra with both too little and too much solvent compensation. Broken lines in the spectra indicate uncertainty in the region of strong solvent absorption. The dioxan solution of maleic acid was 1M and was measured at 0·1 mm., that of potassium hydrogen maleate about 0·1M,

[7] Walker, *J.*, 1892, **61**, 696.
[8] Westheimer and Benfey, *J. Amer. Chem. Soc.*, 1956, **78**, 5309.
[9] Eberson, *Acta Chem. Scand.*, 1959, **13**, 211.

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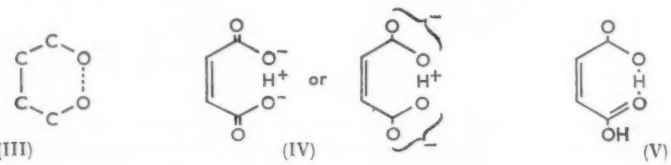
measured at 0·8 mm. thickness. The methanol solution of maleic acid was 0·5M, measured at 0·02 mm.

Results.—The spectra shown in Figs. 2, 3, and 4 cover the carbonyl-stretching and the carboxylate-ion frequencies. The spectra of the solids are subject to the uncertainties of the disc method. Our spectrum of maleic acid agrees with that obtained by Mecke,[10] using the same techniques, and the spectra of the acid and solid potassium hydrogen maleate agree with those obtained by Cardwell, Dunitz, and Orgel,[11] who used Nujol mulls. On the other hand, the spectrum of sodium hydrogen fumarate is entirely different from that given by Hadži and Novak [12] who use Nujol and fluorocarbon mulls. They find, for potassium hydrogen fumarate, a strong band at 1756 cm.$^{-1}$, and their spectrum is shown in Fig. 4. It is possible that the sort of difference that Hadži and Novak find between vitreous and crystalline samples of the acid salt of phenylacetic acid is being observed here.

Discussion.—Both maleic acid [4] and potassium hydrogen maleate [13] have planar ring structures (III) in the crystalline state, with O–O distances (2·46 and 2·42 Å, respectively) which are taken to indicate strong (perhaps symmetrical) hydrogen bonds. Cardwell, Dunitz, and Orgel had argued, before *X*-ray diffraction data were available for potassium hydrogen maleate, that the spectral differences between maleic acid and the acid potassium salt were in favour of the symmetrical structure (IV) for the hydrogen maleate (MH^-) ion. The band (*b*) at 1704 cm.$^{-1}$ in maleic acid, which is due to the externally bonded carbonyl group in the unsymmetrical structure (V), is not present in potassium hydrogen maleate but is found as a broad band centred on 1681 cm.$^{-1}$ in sodium hydrogen fumarate. The broad band extending from 6 to 6·5 μ in maleic acid contains three maxima, of which the first (*c*) at 1632 cm.$^{-1}$ is probably due to C=C stretching (since it appears with varying intensity but fairly constant frequency in all spectra of maleic acid and potassium hydrogen maleate), and the pair (*d*) at about 1585 and 1562 cm.$^{-1}$ can be assigned to vibrations of the C=O link involved in the internal hydrogen bond. The absence of band (*b*) and the considerable lessening of intensity of the C=C band (*c*) in potassium hydrogen maleate is consistent with the symmetrical structure of the HM^- ion. The C=C absorption is not detected in solid sodium hydrogen fumarate, in agreement with the *trans*-configuration. The absorption (*d*) in maleic acid appears in the acid potassium salt at 1569 cm.$^{-1}$, and a further band (*d'*) appears at 1488 cm.$^{-1}$ in the latter. These may also be assigned to C=O/C–O frequencies, possibly coupled with OH deformation, in the symmetrical $\cdot C\overline{O}\cdot O\cdot\cdot H^+\cdot\cdot O\cdot\overline{C}O\cdot$ group. They may be expected to be not far removed from carboxylate



(III) (IV) (V)

frequencies [14] at 1610—1550 and 1420 cm.$^{-1}$. (It is not clear why the carboxylate frequencies do not appear in our spectrum of sodium hydrogen fumarate. The structure of potassium hydrogen fumarate [15] involves an extended chain of hydrogen fumarate [$HFum^-$] ions, externally hydrogen-bonded at each end.) Additional evidence that Cardwell *et al.* might have used is the absence of the very broad absorption between 3500 and 2000 cm.$^{-1}$ from the crystal spectra of potassium hydrogen maleate. This absorption, due to external hydrogen-bonding, is prominent in maleic acid and potassium hydrogen fumarate.

[10] Mecke, D.M.S. Card 5124 (10/59).
[11] Cardwell, Dunitz, and Orgel, *J.*, 1953, 3741.
[12] Hadži and Novak, *Nuovo Cimento*, 1955, **2**, 716.
[13] Darlow, in Hadži (ed.), "Hydrogen Bonding," Pergamon Press, 1959, p. 40.
[14] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, 1954, p. 149.
[15] Gupta, *Acta Cryst.*, 1956, **9**, 263.

Forsen [16] has shown that sodium hydrogen maleate, dissolved in dimethyl sulphoxide, shows proton magnetic resonance signals at very low field and has ascribed this to the internal hydrogen bond which is retained in that solvent. Similar chemical shifts were observed by Eberson and Forsen [17] for solutions in dimethyl sulphoxide of the monoacid salts of the racemic αα′-dialkylsuccinic acids which show high K_1/K_2 ratios in 50% aqueous ethanol. Attempts to find the same chemical shifts in aqueous or methanol solutions of these salts were not successful, but this does not provide evidence against the internal hydrogen bond in these solvents since the signal could be lost by rapid proton exchange between the ion and the solvent. For this reason, the infrared spectrum (where the transitions occur in a time which is shorter than in proton magnetic resonance by a factor of 10^6) is likely to be the only means of obtaining evidence about the stability of the internal hydrogen bond in aqueous solution.

Eberson [18] has compared the spectra of the alkylated succinic acids, their monoacid salts, and solutions of these in methanol and in D_2O. The solid spectra support the view that the monoacid salts of the acids with high K_1/K_2 ratio have the internal hydrogen bond, but that those of the low-ratio acids do not. The externally bonded carbonyl band occurs at 1680—1700 cm.$^{-1}$ but is considerably weakened in the monoacid salts, to a greater extent with the high-ratio acids than the low. The salts of the high-ratio acids also show in the solids the two broad bands near 1580 and 1480 cm.$^{-1}$ which appear to be characteristic of the internally bonded carboxylate groups and correspond to (*d*) and (*d*′) in the spectrum of potassium hydrogen maleate. These bands persisted in methanol and in D_2O solutions (where, however, the species involved would be the deuterated ions).

From Fig. 2 it can be seen that bands (*d*) of maleic acid are not retained in solutions in dioxan or methanol. Furthermore, band (*a*) assigned to the O–H stretching frequency of the internal hydrogen bond in maleic acid is not present in these solutions. The carbonyl frequency (*b*) is prominent at 1724 cm.$^{-1}$ in both solvents. In aqueous solution (*b*) is at 1701 cm.$^{-1}$. The band (*c*) assigned to C=C stretch is present in the solutions but cannot be discerned in water because it is overlapped by the strong band of water itself at 1640 cm.$^{-1}$. It is reasonably certain, however, that the bands (*d*) are not present in aqueous solution. This view is reinforced by the deuterated acid D_2M and its solution in D_2O. Bands (*b*) and (*c*) remain but (*d*) disappears in solution.

In the acid salt the situation is different. Fig. 3 shows that in dioxan solutions of potassium hydrogen maleate the carbonyl band (*b*) appears in medium intensity, the C=C stretching frequency (*c*) is intensified, and the bands (*d*) and (*d*′) are absent. In aqueous solution, however, there is no sign of (*b*), (*c*) is uncertain because of solvent absorption, and the bands (*d*) and (*d*′) remain of high intensity. In the case of potassium deuterium maleate the evidence is similar but somewhat less conclusive.

It appears probable therefore that the intramolecular hydrogen bond present in crystalline maleic acid is not sufficiently strong to withstand competition for the hydrogen bond from dioxan, methanol, or water. The acid maleate ion, on the other hand, has a stronger intramolecular hydrogen bond which remains stable in water but appears to be broken by dioxan. The weak band at 1681 cm.$^{-1}$ in D_2O solutions of potassium deuterium maleate suggests that the bond in that case may be just so stable that both bonded and non-bonded ions are present in comparable equilibrium concentrations.

Chemical Laboratories, King's College,
Newcastle upon Tyne.

[*Received, December 23rd*, 1960.]

[16] Forsen, *J. Chem. Phys.*, 1952, **31**, 852 (1952).
[17] Eberson and Forsen, *J. Phys. Chem.*, 1960, **64**, 767.
[18] Eberson, *Acta Chem. Scand.*, 1959, **13**, 224.

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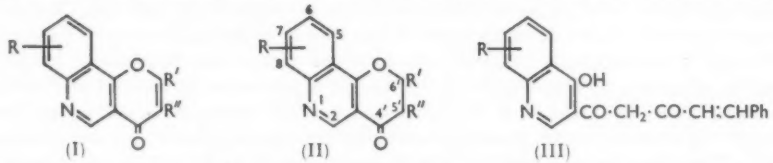
545. *Pyranoquinolines. Part II.*[1]

By K. Elliott and E. Tittensor.

Further examples are described of the synthesis of pyranoquinolines by the application of the Kostanecki–Robinson reaction to derivatives of 3-acetyl-4-hydroxyquinoline. Dihydropyranoquinolines have been prepared by condensing derivatives of 3-acetyl-4-hydroxyquinolines with benzaldehyde.

We have found that in certain cases Snyder and Jones's [2] method for the synthesis of ethyl α-acetyl-β-anilinoacrylates gives only α-acetyl-β-*N*-arylacrylamides, not previously recorded. The acrylates unobtainable by Snyder and Jones's method were, however, prepared by Claisen's method.[3]

The 3-acetyl-4-hydroxyquinolines obtained by thermal cyclisation of the anilinoacrylates in diphenyl ether [2] were heated with various acid anhydrides in the presence of triethylamine. From 3-acetyl-4-hydroxyquinoline and its 6-methoxy- and 6-methyl derivative with benzoic anhydride the sole product, in each case, was the 4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline (I; R = H, OMe, or Me, R′ = Ph, R″ = H), whereas with furoic anhydride the sole product was in each case a 5′-furoyl-6′-furyl-4′-oxo-pyrano-(3′,2′-3,4)quinoline (I; R = H or OMe, or Me, R′ = C_4H_3O, R″ = C_4H_3O·CO). When cinnamic anhydride was used the 6-methoxy-derivative yielded a 5′-cinnamoyl-6′-styrylpyrano(3′,2′-3,4)quinoline (I; R = OMe, R′ = Ph·CH=CH, R″ = Ph·CH=CH·CO), whereas the parent acetylhydroxyquinoline gave the uncyclised product (III; R = H). No product was isolated from the reaction of the 6-methyl derivative with cinnamic anhydride.



No products could be isolated after reaction of 3-acetyl-4-hydroxy-6-, -7-, or -8-nitroquinoline and 3-acetyl-7-chloro-4-hydroxyquinoline with acetic anhydride, but the 5′-acetyl derivatives of the methylpyranoquinolines (I; R = H, Br, OMe, or Me, R′ = Me, R″ = Me·CO) were obtained from 3-acetyl-4-hydroxyquinoline, 3-acetyl-6-bromo-4-hydroxyquinoline, and 3-acetyl-4-hydroxy-6-methoxy- and -6-methyl-quinoline.

The phenyl-, furyl-, and styryl-pyranoquinolines gave the characteristic colours with concentrated sulphuric acid, described in Part 1,[1] whereas the methylpyranoquinolines gave only brown colours.

The ultraviolet absorption spectra of the phenyl- and furyl-pyranoquinolines described above and in Part I are indicated in Table 1. The spectra show a similarity to those of the corresponding naphtho(1′,2′-2,3)pyrans, which are included for comparison. 5-Furoyl-6-furyl-4-oxonaphtho(1′,2′-2,3)pyran, not previously recorded, was prepared by the interaction of 2-acetyl-1-naphthol with furoic anhydride, in the presence of triethylamine.

Condensing 3-acetyl-4-hydroxyquinoline with benzaldehyde in refluxing methanolic sodium hydroxide, cold ethanolic sodium hydroxide [4] or in the presence of piperidine [5] gave only the dihydropyrano(3′,2′-3,4)quinoline (II; R = R″ = H, R′ = Ph). 3-Acetyl-6-bromo-4-hydroxyquinoline condensed with benzaldehyde in refluxing methanolic sodium hydroxide to give a mixture of the dihydropyranoquinoline (II; R = Br, R′ = Ph, R″ = H) and 6-bromo-4-hydroxy-3-quinolyl styryl ketone. When the condensation was carried

[1] Part I, Elliott and Tittensor, *J.*, 1959, 484.
[2] Snyder and Jones, *J. Amer. Chem. Soc.*, 1946, **68**, 1253.
[3] Claisen, *Annalen*, 1897, **297**, 1.
[4] Geissman and Clinton, *J. Amer. Chem. Soc.*, 1946, **68**, 697.
[5] Algar and Hanlon, *Proc. Royal Irish Acad.*, 1929, **38**, *B*, 175.

out in cold ethanolic sodium hydroxide or with piperidine as catalyst the latter compound was the sole product.

TABLE 1. *Ultraviolet spectra* (λ *in* mμ) *for the pyranoquinolines* (I).

R	R′	R″	$\lambda_{max.}$		log ε		$\lambda_{min.}$	log ε
H	Ph	H	222	270	4·56	4·41	240	3·95
7-Cl	Ph	H	230	270	4·38	4·58	240	4·19
6-Br	Ph	H	224	268	4·65	4·56	244	4·26
6-NO_2	Ph	H	224	254	4·35	4·75	—	—
7-NO_2	Ph	H	—	264	—	4·59	230	4·17
8-NO_2	Ph	H	—	268	—	4·42	248	4·17
6-Me	Ph	H	226	272	4·56	4·42	244	3·96
6-OMe	Ph	H	232	266	4·85	4·79	248	4·61
4-Oxo-6-phenylnaphtho(1′,2′-2,3)pyran			252	280	4·67	4·53	263	4·39
6-NO_2	Ph	–COPh	236	262	4·47	3·96	228	4·40
7-NO_2	Ph	–COPh	—	272	—	4·72	—	—
8-NO_2	Ph	–COPh	—	268	—	4·63	236	4·42
5-Benzoyl-4-oxo-6-phenylnaphtho(1′,2′-2,3)pyran			—	268	—	5·16	242	4·19
H	C_4H_3O	C_4H_3O·CO	224	278	4·73	4·61	246	4·26
7-Cl	C_4H_3O	C_4H_3O·CO	230	282	4·57	4·59	250	4·18
6-Br	C_4H_3O	C_4H_3O·CO	232	276	4·31	4·27	250	4·04
6-NO_2	C_4H_3O	C_4H_3O·CO	—	258	—	4·62	—	—
7-NO_2	C_4H_3O	C_4H_3O·CO	—	282	—	4·6	242	4·35
8-NO_2	C_4H_3O	C_4H_3O·CO	222	280	4·54	4·49	244	4·24
6-Me	C_4H_3O	C_4H_3O·CO	228	280	4·63	4·49	248	4·18
6-OMe	C_4H_3O	C_4H_3O·CO	232	276	4·66	4·54	250	4·32
5-Furoyl-6-furyl-4-oxonaphtho-(1′,2′-2,3)pyran			226	284	4·62	4·59	250	4·22

The dihydropyranoquinoline (II; R = Br, R′ = Ph, R″ = H) was recovered unchanged after attempted ozonolysis in chloroform, and no identifiable products were isolated on ozonolysis of the isomeric styryl ketone.

Bromination of 5′,6′-dihydro-4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline (II; R = R″ = H, R′ = Ph) gave the 5′-bromo-derivative which was dehydrobrominated in pyridine to the pyrano(3′,2′-3,4)quinoline (I; R = R″ = H, R′ = Ph). Bromination of either 6-bromo-5′,6′-dihydro-4′-oxo-6-phenylpyrano(3′,2′-3,4)quinoline or the 6-bromo-4-hydroxy-3-quinolyl styryl ketone gave the 5′,6-dibromophenylpyrano(3′,2′-3,4)quinoline (II; R = R″ = Br, R′ = Ph), which was dehydrobrominated to 6-bromo-4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline (I; R = Br, R′ = Ph, R″ = H).

5′,6′-Dihydro-4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline and its 6-bromo-derivative were dehydrogenated by *N*-bromosuccinimide [6] or selenium dioxide [7] to 4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline (I; R = R″ = H, R′ = Ph) and the 6-bromo-compound (I; R = Br, R′ = Ph, R″ = H) respectively. Treatment of 6-bromo-4-hydroxy-3-quinolyl styryl ketone with selenium dioxide caused simultaneous cyclisation and dehydrogenation, yielding 6-bromo-4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline (I; R = Br, R′ = Ph, R″ = H).

The action of pentyl nitrite [8] on 5′,6′-dihydro-4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline and the 6-bromodihydropyranoquinoline (II; R = Br, R′ = Ph, R″ = H) gave in both cases the 5′-hydroxyimino-compound (II; R = H or Br, R′ = Ph, R″ = :N·OH) which was hydrolysed in 50% sulphuric acid to the corresponding 5′-hydroxy-compound. Treatment of 5′,6′-dihydro-4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline (II; R = R″ = H, R′ = Ph) with alkaline hydrogen peroxide [9] gave directly 5′-hydroxy-4′-oxo-6′-phenylpyrano-(3′,2′-3,4)quinoline (I; R = H, R′ = Ph, R″ = OH). Under similar conditions 6-bromo-5′,6′-dihydro-4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline and 6-bromo-4-hydroxy-3-quinolyl

[6] Lorette, Gage, and Wender, *J. Org. Chem.*, 1951, **16**, 930.
[7] Mahal, Rai, and Venkataraman, *J.*, 1935, 866.
[8] Kostanecki and Lampe, *Ber.*, 1904, **37**, 773.
[9] Oyamada, *J. Chem. Soc. Japan*, 1934, **55**, 1256.

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styryl ketone gave 6-bromo-5′-hydroxy-4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline (I; R = Br, R′ = Ph, R″ = OH).

Experimental

Ethyl α-Acetyl-β-anilinoacrylates and α-Acetyl-β-anilino-N-phenylacrylamides.—The anilinoacrylates prepared by Snyder and Jones's method [2] (cf. Part I [1]) are recorded in Table 2, nos. 1—3. The corresponding acrylamides, obtained simultaneously, are shown in Table 3, nos. 1—3. Only the acrylamides were isolated in experiments 4—11 of Table 3. Ethyl α-acetyl-β-anilino-, -*p*-anisidino-, and -*p*-toluidino-acrylate (Table 2, nos. 12—14) were prepared by Claisen's method.[3]

Table 2. *Ethyl α-acetyl-β-anilinoacrylates*, R·C_6H_4·NH·CH:CAc·CO_2Et.

				Required (%)				Found (%)		
No.	R	Solvent	M. p.	C	H	N	Formula	C	H	N
1	*p*-Cl	A	87—89°	58·3	5·2	5·2	$C_{13}H_{14}ClNO_3$	58·2	5·0	5·3
2	*o*-Br	B	92—94	50·0	4·5	4·5	$C_{13}H_{14}BrNO_3$	50·0	4·4	4·8
3	*m*-Br	B	94—96	50·0	4·5	4·5	$C_{13}H_{14}BrNO_3$	50·0	4·6	4·8
Prepared by Claisen's method:										
12	H	D	41—43	—	—	—		—	—	—
13	*p*-Me	D	50—51	68·0	6·8	5·7	$C_{14}H_{17}NO_3$	68·0	7·0	5·9
14	*p*-OMe	A	87—88	—	—	—		—	—	—

A, MeOH. B, EtOH. C, Toluene. D, Light petroleum (b. p. 60—80°).

Table 3. *α-Acetyl-β-anilino-N-arylacrylamides*, R·C_6H_4·NH·CH:CAc·CO·NH·C_6H_4R.

				Required (%)				Found (%)		
No.	R	Solvent	M. p.	C	H	N	Formula	C	H	N
1	*p*-Cl	C	202—204°	58·5	4·0	8·0	$C_{17}H_{14}Cl_2N_2O_2$	58·8	4·3	8·2
2	*o*-Br	C	163—165	46·5	3·2	6·4	$C_{17}H_{14}Br_2N_2O_2$	46·9	3·2	6·3
3	*m*-Br	C	155—156	46·5	3·2	6·4	,,	46·9	3·1	6·5
4	H	A	156—157	72·7	5·7	10·0	$C_{17}H_{16}N_2O_2$	72·7	5·6	11·2, 11·0
5	*o*-Cl	A	136—138	58·5	4·0	8·0	$C_{17}H_{14}Cl_2N_2O_2$	58·5	4·0	8·4
6	*o*-Me	B	170—171	74·0	6·5	9·1	$C_{19}H_{20}N_2O_2$	73·7	6·2	9·0
7	*m*-Me	B	132—134	,,	,,	,,	,,	74·0	6·6	9·4
8	*p*-Me	B	174—175	,,	,,	,,	,,	74·1	6·6	9·4
9	*o*-OMe	B	139—141	67·1	5·9	8·2	$C_{19}H_{20}N_2O_4$	66·9	5·9	8·1
10	*m*-OMe	B	137—139	,,	,,	,,	,,	67·3	5·8	8·2
11	*p*-OMe	A	130—132	,,	,,	,,	,,	67·3	5·8	7·9

A—D, as in Table 2.

3-Acetyl-4-hydroxyquinolines.—3-Acetyl-4-hydroxyquinoline and 3-acetyl-4-hydroxy-6-methyl- and -6-methoxy-quinoline were prepared as described in Part I.

4′-Oxo-6′-phenylpyrano(3′,2′-3,4)quinoline.—3-Acetyl-4-hydroxyquinoline (1·8 g.) was refluxed with benzoic anhydride (11·3 g.) and triethylamine (8·3 c.c.) at 170—180° for 2 hr., the cooled mixture extracted with ether (50 c.c.), and the insoluble material (0·9 g.) crystallised from ethanol, to give *4′-oxo-6′-phenylpyrano(3′,2′-3,4)quinoline*, needles, m. p. 231—232° (Found: C, 78·6; H, 4·0; N, 5·4. $C_{18}H_{11}NO_2$ requires C, 79·1; H, 4·0; N, 5·1%).

Similarly 3-acetyl-4-hydroxy-6-methyl- and -6-methoxy-quinoline at 170—180° (2 and 3 hr., respectively) gave the following ether-insoluble 4′-oxo-6′-phenylpyranoquinolines; *6-methyl-*, needles (from ethanol), m. p. 216—218° (Found: C, 79·3; H, 4·5; N, 4·9. $C_{19}H_{13}NO_2$ requires C, 79·5; H, 4·5; N, 4·9%), *6-methoxy-*, needles (from ethanol), m. p. 202—204° (Found: C, 75·7; H, 4·4; N, 4·4. $C_{19}H_{13}NO_3$ requires C, 75·3; H, 4·3; N, 4·6%).

3-Cinnamoylacetyl-4-hydroxyquinoline.—3-Acetyl-4-hydroxyquinoline (1·8 g.), cinnamic anhydride (13·9 g.), and triethylamine (8·5 c.c.) were refluxed at 190—200° for 3 hr. The tarry mixture was extracted with ether, and the insoluble material crystallised from propanol, to give *3-cinnamoylacetyl-4-hydroxyquinoline*, prisms, m. p. 210—214° (decomp.) (Found: C, 76·9; H, 4·6; N, 4·7. $C_{20}H_{15}NO_3$ requires C, 76·0; H, 4·7; N, 4·4%).

5′-Cinnamoyl-6-methoxy-4′-oxo-6′-styrylpyrano(3′,2′-3,4)quinoline.—3-Acetyl-4-hydroxy-6-methoxyquinoline (2·2 g.) was refluxed with cinnamic anhydride (13·9 g.) and triethylamine (8·3 c.c.) at 190—200° for 3·5 hr., the cooled mixture extracted with methanol, and the insoluble

material (0·3 g.) crystallised from 2-ethoxyethanol to give *5'-cinnamoyl-6-methoxy-4'-oxo-6'-styrylpyrano(3',2'-3,4)quinoline* as yellow needles, m. p. 250—252° (Found: C, 79·0; H, 4·6; N, 2·8. $C_{30}H_{21}NO_4$ requires C, 78·6; H, 4·6; N, 3·0%).

5'-Furoyl-6'-furyl-4'-oxopyrano(3',2'-3,4)quinoline.—3-Acetyl-4-hydroxyquinoline (1·8 g.) was refluxed with furoic anhydride (10·3 g.) and triethylamine (8·3 c.c.) at 170—180°, for 2 hr., the black oil diluted with acetone, and the precipitated solid (1·6 g.) crystallised from nitrobenzene, to give *5'-furoyl-6'-furyl-4'-oxopyrano(3',2'-3,4)quinoline* as needles, m. p. 278—279° (Found: C, 70·4; H, 3·1; N, 4·3. $C_{21}H_{11}NO_5$ requires C, 70·6; H, 3·1; N, 3·9%).

Similarly 3-acetyl-4-hydroxy-6-methyl- and -6-methoxy-quinoline, reacting at 170—180° for 2 hr., gave the *6-methyl-*, needles (from acetic acid), m. p. >300° (Found: C, 71·3; H, 3·5; N, 3·9. $C_{22}H_{13}NO_5$ requires C, 71·0; H, 3·5; N, 3·8%), and the *6-methoxy*-derivative, needles (from 2-ethoxyethanol), m. p. >300° (Found: C, 67·6; H, 3·5; N, 3·4. $C_{22}H_{13}NO_6$ requires C, 68·2; H, 3·4; N, 3·6%).

5'-Acetyl-6'-methyl-4'-oxopyrano(3',2'-3,4)quinoline.—3-Acetyl-4-hydroxyquinoline (1·8 g.), acetic anhydride (9·4 c.c.), and triethylamine (8·3 c.c.) were refluxed at 180—190° for 6 hr. The cooled mixture was diluted with ether, and the light brown solid collected and treated with 2N-sodium hydroxide. The insoluble material crystallised from propanol, giving *5'-acetyl-6'-methyl-4'-oxopyrano(3',2'-3,4)quinoline* (0·7 g.) as prisms, m. p. 270—275° (decomp.) (Found: C, 71·8; H, 4·4; N, 5·3. $C_{15}H_{11}NO_3$ requires C, 71·2; H, 4·4; N, 5·5%).

Similarly 3-acetyl-6-bromo-4-hydroxyquinoline and 3-acetyl-4-hydroxy-6-methyl- and -6-methoxy-quinoline gave the *6-bromo-* (prepared at 160—170°; 3 hr.), prisms (from aqueous ethanol), m. p. 275—277° (Found: C, 54·0; H, 3·1; N, 4·8. $C_{15}H_{10}BrNO_3$ requires C, 54·2; H, 3·0; N, 4·2%), *6-methyl-* (prepared at 210—220°; 7·5 hr.), prisms (from propanol), m. p. >300° (Found: C, 72·3; H, 5·1; N, 4·6. $C_{16}H_{13}NO_3$ requires C, 71·9; H, 4·9; N, 5·2%), and *6-methoxy-analogue* (prepared at 210—220°; 6 hr.), prisms (from cyclohexanol), m. p. >300° (Found: C, 67·4; H, 4·8; N, 4·7. $C_{16}H_{13}NO_4$ requires C, 67·8; H, 4·6; N, 5·0%).

Condensation of 3-Acetyl-4-hydroxyquinoline with Benzaldehyde.—(a) *In hot methanolic sodium hydroxide.* 3-Acetyl-4-hydroxyquinoline (1·0 g.), methanol (10·0 c.c.), 10% aqueous sodium hydroxide (20 c.c.), and benzaldehyde (2·5 c.c.) were refluxed for 0·5 hr. After acidification of the cooled solution the precipitate was collected and crystallised from propanol, to give *5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline* as prisms, m. p. 269—271° (Found: C, 78·6; H, 5·0; N, 5·2. $C_{18}H_{13}NO_2$ requires C, 78·5; H, 4·8; N, 5·1%).

(b) *In cold alcoholic sodium hydroxide.* A suspension of 3-acetyl-4-hydroxyquinoline (1·0 g.) in 60% sodium hydroxide (14 c.c.) was treated with ethanol (50 c.c.) and benzaldehyde (0·59 c.c.). The mixture was kept at 0—5° for 48 hr. and then acidified. The precipitate was crystallised from propanol, giving 5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline, m. p. and mixed m. p. 269—271°.

(c) *In the presence of piperidine.* A solution of 3-acetyl-4-hydroxyquinoline (1·0 g.), benzaldehyde (0·59 c.c.), and piperidine (2·9 c.c.) in ethanol (25 c.c.) was refluxed for 3·75 hr. A bright yellow precipitate was slowly deposited. The solid crystallised from propanol, giving the same dihydropyranoquinoline as described in (a) above (m. p. and mixed m. p. 269—271°).

Condensation of benzaldehyde with 3-acetyl-6-bromo-4-hydroxyquinoline under the conditions described in (a) gave as the main product *6-bromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline* as prisms (from propanol), m. p. 290—292° (Found: C, 60·8; H, 3·5; N, 4·1. $C_{18}H_{12}BrNO_2$ requires C, 61·0; H, 3·4; N, 4·0%) (isolated as a sodium salt).

Dilution and acidification of the methanolic filtrate gave a brown precipitate which crystallised from 2-ethoxyethanol, giving *6-bromo-4-hydroxy-3-quinolyl styryl ketone* as prisms, m. p. 270—271° (Found: C, 60·8; H, 3·5; N, 4·2. $C_{18}H_{12}BrNO_2$ requires C, 61·0; H, 3·4; N, 4·0%).

5',6-Dibromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline.—(*a*) A suspension of 6-bromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline (2·3 g.) in chloroform (50 c.c.) was treated with bromine (1·04 g.) in chloroform (25 c.c.), and then the pale yellow solution was evaporated. The residual gum crystallised from methanol, giving *5',6-dibromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline* (2·8 g.) as prisms, m. p. 260° (decomp.) (Found: Br, 37·0. $C_{18}H_{11}Br_2NO_2$ requires Br, 36·8%).

(*b*) A solution of bromine (0·18 c.c.) in chloroform (15 c.c.) was added to a suspension of 6-bromo-4-hydroxy-3-quinolyl styryl ketone (0·5 g.) in chloroform (15 c.c.). Evaporation gave a glass which crystallised from ethanol, giving the preceding compound, m. p. 258—260° (decomp.) (Found: Br, 36·6%).

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5'-Bromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline.—Bromination of 5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline as above gave the *5'-bromo-derivative* as prisms, m. p. >300° (Found: Br, 23·2. $C_{18}H_{12}BrNO_2$ requires Br, 22·6%).

6-Bromo-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline.—(a) *Dehydrobromination with pyridine.* A solution of 5',6-dibromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline (0·2 g.) in pyridine (1·5 c.c.) was heated at 95° for 15 min. On cooling, 6-bromo-4'-oxo-6'-phenylpyrano-(3',2'-3,4)quinoline was deposited as needles, m. p. and mixed m. p. 228—230°

(b) *N-Bromosuccinimide.* 6-Bromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline (0·5 g.), *N*-bromosuccinimide (0·3 g.), benzoyl peroxide (0·02 g.), and acetic acid (25 c.c.) were refluxed for 1·5 hr. The cooled solution was diluted with water (100 c.c.) and kept for 3 days. The precipitate was collected and extracted with chloroform. Evaporation then gave 6-bromo-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline, m. p. and mixed m. p. 229—231°.

(c) *Selenium dioxide.* Selenium dioxide (0·55 g.), 6-bromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline (0·5 g.), and dioxan (10 c.c.) were refluxed for 1·75 hr. The hot mixture was filtered and the dioxan evaporated. Trituration of the residual gum with ethanol gave the preceding compound (0·2 g.), m. p. and mixed m. p. 229—231°.

(d) Treatment of 6-bromo-4-hydroxyquinolyl styryl ketone (0·5 g.) with selenium dioxide (0·5 g.) as in (c) gave the same 6-bromo-compound, m. p. and mixed m. p. 228—230°.

4'-Oxo-6'-phenylpyrano(3',2'-3,4)quinoline.—Treatment of 5'-bromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2',3,4)quinoline as in (a) above gave 4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline, m. p. and mixed m. p. 230—232°.

4'-Oxo-6'-phenylpyrano(3',2'-3,4)quinoline, m. p. and mixed m. p. 230—232°, was also obtained when 5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline was treated with *N*-bromosuccinimide or selenium dioxide as described above.

5'-Hydroxy-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline and its 6-Bromo-derivative.—(a) *Hydrogen peroxide.* A suspension of 5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline (0·55 g.) in a mixture of N-sodium hydroxide (2 c.c.) and ethanol (20 c.c.) was treated with 30% hydrogen peroxide (1 c.c.). The solution was kept at room temperature for 24 hr., then acidified. The precipitate crystallised from aqueous dioxan, giving *5'-hydroxy-4'-oxo-6'-phenylpyrano-(3',2'-3,4)quinoline* as prisms, m. p. 290—292° (Found: C, 74·4; H, 4·1; N, 5·5. $C_{18}H_{11}NO_3$ requires C, 74·8; H, 3·8; N, 4·9%).

Similarly 6-bromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline and 6-bromo-4-hydroxy-3-quinolyl styryl ketone gave *6-bromo-5'-hydroxy-4'-oxo-6'-phenylpyrano(3',2'-3,4)-quinoline*, needles (from pyridine), m. p. 299—300° (Found: C, 58·4; H, 3·3; N, 3·8. $C_{18}H_{10}BrNO_3$ requires C, 58·7; H, 2·7; N, 3·8%).

(b) *Through the hydroxyimino-derivative.* Hydrochloric acid (10 c.c.) was added to a suspension of 5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline (1·0 g.) in a solution of pentyl nitrite (5 c.c.) in ethanol (25 c.c.). After 3 hr. at room temperature the mixture was basified with ammonia. The yellow precipitate was collected and crystallised from ethanol, giving *5',6'-dihydro-5'-hydroxyimino-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline* as prisms, m. p. 190—191° (decomp.) (Found: C, 71·2; H, 4·1; N, 9·6. $C_{18}H_{12}N_2O_3$ requires C, 71·0; H, 4·0; N, 9·2%).

Hydrolysis of this product in refluxing 50% w/v sulphuric acid during 1·5 hr. gave 5'-hydroxy-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline, needles, m. p. and mixed m. p. 290—292°.

Similarly 6-bromo-5',6'-dihydro-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline gave *6-bromo-5',6'-dihydro-5'-hydroxyimino-4'-oxo-6'-phenylpyrano(3',2'-3,4)quinoline*, prisms (from ethanol), m. p. 199—200° (decomp.) (Found: C, 56·1; H, 3·1; N, 7·1. $C_{18}H_{11}BrN_2O_3$ requires C, 56·4; H, 2·9; N, 7·3%).

Hydrolysis of the hydroxyimino-compound gave the 5'-hydroxy-compound, needles (from pyridine), m. p. and mixed m. p. 299—300° (Found: C, 58·4; H, 3·3; N, 3·8. Calc. for $C_{18}H_{10}BrNO_3$: C, 58·7; H, 2·7; N, 3·8%).

5-Furoyl-6-furyl-4-oxonaphtho(1',2'-2,3)pyran.—2-Acetyl-1-naphthol (3·7 g.), furoic anhydride (10·3 g.), and triethylamine (8·3 c.c.) were refluxed at 170—180° for 2 hr. The cooled black oil was treated with a mixture of ether and acetone (9 : 1; 10 c.c.). The precipitate was crystallised from ethanol, giving *5-furoyl-6-furyl-4-oxonaphtho(1',2'-2,3)pyran* as needles, m. p. 222—224° (Found: C, 73·4; H, 3·6. $C_{22}H_{12}O_5$ requires C, 74·1; H, 3·4%).

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HUDDERSFIELD COLLEGE OF TECHNOLOGY.

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Vol. 1961, page 2801. *For* *N*-ethyl-2,2′- *read* *N*-ethyl-2,2- *throughout the paper.*

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546. *The Stereochemistry of Molecules Containing the* C=C=N *Group. Part III.*[1] *The Crystal and Molecular Structure of* N-*Ethyl*-2,2′-*dimethylsulphonylvinylideneamine.*

By J. J. Daly.

A three-dimensional structural analysis of a third compound containing the >C=C=NR group is described. Crystals of *N*-ethyl-2,2′-dimethylsulphonylvinylideneamine are orthorhombic $P2_12_12_1$ with $a = 12{\cdot}02$, $b = 5{\cdot}85$, $c = 14{\cdot}47$ Å. The bond angle at the nitrogen atom is 144°, in sharp contrast to the value of 180° found in two other vinylideneamines in which R = Me. The bond lengths and other bond angles exhibit no unusual features, except the C=N bond which has the length of a normal C≡N bond. It is suggested that the linearity of the −N= system in *N*-methylvinylideneamines is due, at least partly, to hyperconjugation.

It has been shown in Parts I [2] and II [1] that the −N= system in two *N*-methylvinylideneamines is linear. In order for this system to achieve linearity the lone pair of electrons on the nitrogen atom must be absorbed into the rest of the molecule. In Part II it was suggested that hyperconjugation or electronegativity, or both, might account for the transfer of the lone pair. In an attempt to assess the relative importance of these two effects the crystal structure of *N*-ethyl-2,2′-dimethylsulphonylvinylideneamine, $(CH_3{\cdot}SO_2)_2C{=}C{=}NEt$, has been determined. Although some doubt has recently been cast on the importance of the part played by hyperconjugation in the ground state of molecules,[3,4] the results of the analysis show that hyperconjugation must play some part in the bonding of *N*-methylvinylideneamines.

Experimental.—The synthesis of *N*-ethyl-2,2′-dimethylsulphonylvinylideneamine will be described separately.[5]

Molecular formula: $C_6H_{11}O_4S_2N$, $M = 225{\cdot}29$. Orthorhombic, $a = 12{\cdot}02 \pm 0{\cdot}04$ Å, $b = 5{\cdot}85 \pm 0{\cdot}02$ Å, $c = 14{\cdot}47 \pm 0{\cdot}04$ Å. $U = 1017$ Å^3. $D_m = 1{\cdot}44$ g./c.c. (by flotation), $Z = 4$, $D_c = 1{\cdot}44$ g./c.c. $F(000) = 472$. Space group $P2_12_12_1$ (D_2^4 No. 41), origin at 1/4,1/4,1/4 from the Int. Tab. origin.[6] Cu-K_α radiation, $\mu = 44{\cdot}3$ cm.$^{-1}$, single crystal oscillation and Weissenberg photographs about the *a*, *b*, and *c* axes. No correction was made for absorption.

The relative intensities of 1120 reflections were estimated by eye from a calibration strip and were placed on the same scale by equating $\sum|F_o|$ in common reciprocal rows. An approximate scale and temperature factor were obtained from *h*0*l* intensities by the method of Howells, Phillips, and Rogers.[7] A further 176 reflections, the intensities of which were too low to be observed, were given a value of one-half of the minimum observable intensity and are included in the *R*-values quoted.

The *R*-value used in this paper is the residual $\dfrac{\sum\big||F_o| - |F_c|\big|}{\sum|F_o|}$.

Structure determination. The positions of the sulphur atoms were determined from the Patterson functions of the *a*- and *b*-axis projections. Fourier methods (in projection) were then used to obtain a complete set of co-ordinates. An attempt was made to refine these co-ordinates three-dimensionally by using 390 low-order planes. The least-squares method was used and the calculations were done on the Leeds University Pegasus computer. The programmes were devised by Dr. D. W. J. Cruickshank and Miss D. E. Pilling. The weights used were $w = 1$ throughout.

After four refinement cycles the residual fell slowly to 0·27, so the calculated phase angles were used to evaluate the electron density in three dimensions. This electron density showed that sites of the carbon atoms of the ethyl group (C5 and C6; see Fig. 1) were in error. New

[1] Part II, Bullough and Wheatley, *Acta Cryst.*, 1957, **10**, 233.
[2] Wheatley, *Acta Cryst.*, 1954, **7**, 68.
[3] Rao, *Nature*, 1960, **187**, 913.
[4] Dewar and Schmeising, *Tetrahedron*, 1959, **5**, 166.
[5] Challenger, unpublished work.
[6] "International Tables for X-Ray Crystallography," Vol. I, Kynoch Press, Birmingham, 1952.
[7] Howells, Phillips, and Rogers, *Acta Cryst.*, 1950, **3**, 210.

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positions were found for these atoms and the trial structure thus produced was eventually refined by using all 1296 intensities. The final value of the residual (after anisotropic refinement of the temperature factors) was 0·10.

Results.—The results of the analysis are summarized in the Tables and Figures.

TABLE 1. *Final co-ordinates* (Å) *for* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$.

	x	*y*	*z*		*x*	*y*	*z*
S 1	7·6002	1·2262	8·1286	C 1	7·1234	2·6999	8·9912
S 2	5·1042	0·9074	6·4295	C 2	4·9572	−0·8507	6·5980
O 1	9·0194	1·2757	7·8849	C 3	6·7959	1·2852	6·5881
O 2	4·7436	1·2630	5·0811	C 4	7·4642	1·5700	5·4431
O 3	7·0605	0·1090	8·8447	C 5	8·4458	2·6217	3·3902
O 4	4·4080	1·5310	7·5144	C 6	7·6254	3·9130	3·4620
N 1	8·0475	1·6813	4·4405				

FIG. 1. *Numbering of the atoms and the bond lengths in* $(CH_3{\cdot}SO_2)_2C{=}C{=}NEt$.

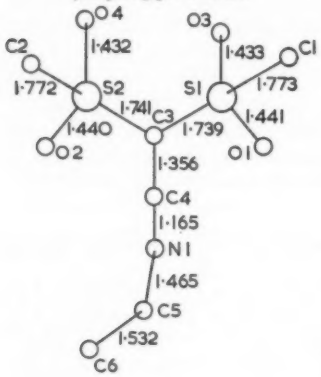

FIG. 2. *The unit cell contents viewed down the b-axis, and some of the more important van der Waals distances.*

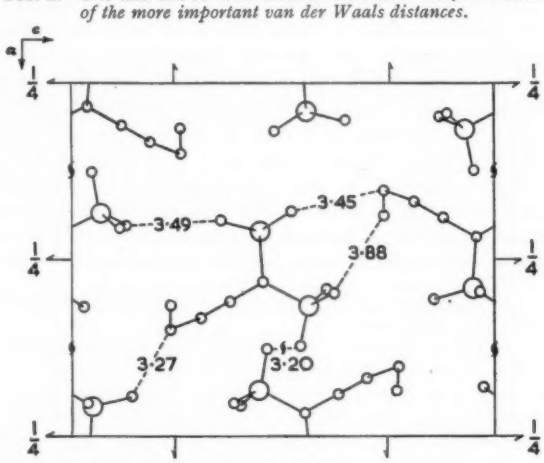

TABLE 2. U_{ij} (Å²) *for* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$.

	U_{11}	U_{22}	U_{33}	$2U_{12}$	$2U_{23}$	$2U_{13}$
S 1	0·0375	0·0388	0·0404	0·0032	0·0075	−0·0037
S 2	0·0343	0·0698	0·0492	−0·0014	0·0164	−0·0085
O 1	0·0385	0·0602	0·0581	0·0089	0·0053	−0·0156
O 2	0·0563	0·1131	0·0659	−0·0247	0·0451	−0·0470
O 3	0·0670	0·0428	0·0466	−0·0111	0·0252	−0·0025
O 4	0·0437	0·0860	0·0678	0·0180	−0·0033	0·0201
N 1	0·0482	0·0734	0·0397	−0·0270	−0·0101	0·0064
C 1	0·0616	0·0485	0·0584	0·0052	−0·0118	−0·0042
C 2	0·0694	0·0567	0·0923	−0·0182	−0·0177	−0·0035
C 3	0·0466	0·0559	0·0423	−0·0069	0·0155	−0·0113
C 4	0·0435	0·0503	0·0511	0·0048	0·0078	−0·0069
C 5	0·0661	0·0800	0·0434	−0·0386	0·0160	0·0167
C 6	0·0691	0·0846	0·0821	−0·0161	0·0308	−0·0433

TABLE 3. *Standard deviations* (Å) *of the co-ordinates and* σ_{rms} *for* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$.

	x	*y*	*z*	σ_{rms}		*x*	*y*	*z*	σ_{rms}
S 1	0·0023	0·0025	0·0025	0·0024	C 1	0·0121	0·0117	0·0117	0·0118
S 2	0·0025	0·0032	0·0029	0·0029	C 2	0·0129	0·0129	0·0143	0·0134
O 1	0·0064	0·0079	0·0070	0·0071	C 3	0·0096	0·0113	0·0095	0·0102
O 2	0·0079	0·0113	0·0081	0·0092	C 4	0·0098	0·0111	0·0101	0·0103
O 3	0·0081	0·0076	0·0071	0·0076	C 5	0·0125	0·0143	0·0111	0·0127
O 4	0·0071	0·0098	0·0078	0·0083	C 6	0·0132	0·0158	0·0136	0·0142
N 1	0·0084	0·0110	0·0080	0·0093					

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TABLE 4. *Bond lengths and bond angles, and their standard deviations in* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$.

Bond	Length (Å)	σ (Å)	Angle	Size	(σ)	Angle	Size	(σ)
S1–O1	1·441	0·0075	S1–C3–S2	121° 32′	0° 36′	O2–S2–C2	108° 15′	0° 35′
S2–O2	1·440	0·0097	S1–C3–C4	121° 49′	0° 48′	O2–S2–C3	105° 58′	0° 31′
S1–O3	1·433	0·0080	S2–C3–C4	116° 36′	0° 47′	O3–S1–C1	107° 41′	0° 31′
S2–O4	1·432	0·0088	N1–C4–C3	173° 21′	1° 08′	O3–S1–C3	107° 10′	0° 30′
S1–C1	1·773	0·0121	N1–C5–C6	111° 13′	1° 02′	O4–S2–C2	108° 38′	0° 34
S2–C2	1·772	0·0137	O1–S1–O3	118° 51′	0° 27′	O4–S2–C3	108° 00′	0° 30′
S1–C3	1·739	0·0104	O1–S1–C1	108° 35′	0° 30′	C1–S1–C3	106° 10′	0° 31′
S2–C3	1·741	0·0106	O1–S1–C3	107° 44′	0° 28′	C2–S2–C3	106° 42′	0° 34′
N1–C4	1·165	0·0139	O2–S2–O4	118° 41′	0° 32′	C4–N1–C5	144° 31′	1° 03′
N1–C5	1·465	0·0157						
C3–C4	1·356	0·0145						
C5–C6	1·532	0·0191						

TABLE 5. *Standard deviations* (Å^2) *of the* U_{ij} *for* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$.

	U_{11}	U_{22}	U_{33}	$2U_{12}$	$2U_{23}$	$2U_{13}$
S 1	0·0010	0·0011	0·0011	0·0019	0·0019	0·0018
S 2	0·0011	0·0017	0·0013	0·0025	0·0028	0·0021
O 1	0·0032	0·0044	0·0042	0·0070	0·0081	0·0066
O 2	0·0046	0·0079	0·0049	0·0120	0·0117	0·0084
O 3	0·0046	0·0039	0·0039	0·0079	0·0070	0·0074
O 4	0·0038	0·0062	0·0048	0·0093	0·0104	0·0075
N 1	0·0045	0·0064	0·0043	0·0104	0·0098	0·0077
C 1	0·0066	0·0060	0·0065	0·0121	0·0115	0·0118
C 2	0·0074	0·0071	0·0093	0·0134	0·0150	0·0148
C 3	0·0050	0·0059	0·0050	0·0101	0·0102	0·0088
C 4	0·0049	0·0057	0·0053	0·0103	0·0104	0·0090
C 5	0·0072	0·0096	0·0059	0·0151	0·0136	0·0114
C 6	0·0078	0·0100	0·0088	0·0160	0·0176	0·0146

TABLE 6. *Minimum van der Waals contacts* (Å) *in* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$.

O–O	C–O	C–C	O–N	C–N
3·2	3·3	3·9	3·4	3·6

TABLE 7. *List of* $|F_o|$, $|F_c|$, A_c, *and* B_c *(for N-ethyl-2,2′-dimethylsulphonylvinylideneamine) on ten times the absolute scale.*

h	k	l	$\|F_o\|$	$\|F_c\|$	A_c	B_c
0	0	2	1058	1138	1138	0
0	0	4	151	129	129	0
0	0	6	475	449	−449	0
0	0	8	400	349	−349	0
0	0	10	503	502	−502	0
0	0	12	305	279	−279	0
0	0	14	26	3	3	0
0	0	16	226	197	197	0
0	0	18	116	116	116	0
1	0	1	412	458	0	458
1	0	2	170	207	0	207
1	0	3	180	158	0	−158
1	0	4	63	30	0	30
1	0	5	382	345	0	−345
1	0	6	289	293	0	293
1	0	7	235	218	0	−218
1	0	8	323	304	0	304
1	0	9	123	122	0	−122
1	0	10	67	72	0	−72
1	0	11	25	16	0	16
1	0	12	93	83	0	−83
1	0	13	166	151	0	−151
1	0	14	106	88	0	−88
1	0	15	96	102	0	+102
1	0	16	22	24	0	−24
1	0	17	47	42	0	42
1	0	18	56	65	0	−65
2	0	0	179	164	164	0
2	0	1	165	203	203	0
2	0	2	439	397	397	0
2	0	3	1293	1337	1337	0
2	0	4	379	352	−352	0
2	0	5	222	211	211	0
2	0	6	79	55	−55	0
2	0	7	111	118	118	0
2	0	8	20	29	−29	0
2	0	9	103	97	−97	0
2	0	10	48	69	−69	0
2	0	11	314	310	−310	0
2	0	12	61	55	−55	0
2	0	13	302	284	−284	0
2	0	14	25	3	3	0
2	0	15	107	108	−108	0
2	0	16	21	19	19	0
2	0	17	26	32	−32	0
2	0	18	47	41	41	0
3	0	1	341	315	0	−315
3	0	2	149	141	0	141
3	0	3	530	485	0	−485
3	0	4	595	634	0	634
3	0	5	447	438	0	−438
3	0	6	396	389	0	389
3	0	7	20	39	0	39
3	0	8	6	14	0	14
3	0	9	355	365	0	365
3	0	10	34	27	0	−27
3	0	11	135	102	0	102
3	0	12	213	191	0	−191
3	0	13	26	23	0	−23
3	0	14	26	2	0	−2
3	0	15	29	15	0	15
3	0	16	46	51	0	−51
3	0	17	47	45	0	45
3	0	18	48	46	0	46
4	0	0	1340	1397	−1397	0
4	0	1	705	678	678	0
4	0	2	340	335	−335	0
4	0	3	280	250	250	0
4	0	4	225	208	208	0
4	0	5	112	150	150	0
4	0	6	129	126	126	0
4	0	7	21	39	39	0
4	0	8	89	57	57	0
4	0	9	8	20	20	0
4	0	10	151	142	142	0
4	0	11	26	7	−7	0
4	0	12	87	65	65	0
4	0	13	56	62	−62	0
4	0	14	81	80	−80	0
4	0	15	92	73	−73	0
4	0	16	139	130	−130	0
4	0	17	16	1	−1	0
4	0	18	31	55	−55	0
5	0	1	151	139	0	−139
5	0	2	55	47	0	−47
5	0	3	118	105	0	105
5	0	4	29	33	0	−33
5	0	5	179	159	0	159
5	0	6	127	134	0	−134
5	0	7	389	368	0	368
5	0	8	183	173	0	−173
5	0	9	308	297	0	297
5	0	10	26	21	0	−21
5	0	11	26	34	0	34
5	0	12	159	153	0	153
5	0	13	26	38	0	−38
5	0	14	25	4	0	−4
5	0	15	160	154	0	−154
5	0	16	46	44	0	44
5	0	17	94	93	0	−93
6	0	0	630	664	−664	0
6	0	1	173	151	−151	0
6	0	2	517	508	−508	0
6	0	3	215	194	−194	0
6	0	4	166	176	176	0
6	0	5	116	111	−111	0
6	0	6	165	145	145	0
6	0	7	78	64	−64	0
6	0	8	91	83	83	0
6	0	9	75	66	66	0
6	0	10	260	247	247	0
6	0	11	170	152	152	0
6	0	12	173	148	148	0
6	0	13	105	104	104	0
6	0	14	68	58	58	0
6	0	15	21	27	27	0
6	0	16	18	11	−11	0

XUM

TABLE 7. (*Continued.*)

h	k	l	$\|F_o\|$	$\|F_c\|$	A_c	B_c
6	0	17	11	6	6	0
7	0	1	156	127	0	−127
7	0	2	268	262	0	−262
7	0	3	60	68	0	−68
7	0	4	591	607	0	−607
7	0	5	230	234	0	234
7	0	6	535	562	0	−562
7	0	7	115	97	0	97
7	0	8	227	221	0	−221
7	0	9	71	49	0	−49
7	0	10	176	164	0	164
7	0	11	36	56	0	56
7	0	12	80	215	0	215
7	0	13	24	4	0	4
7	0	14	129	111	0	111
7	0	15	19	17	0	−17
7	0	16	38	39	0	39
8	0	0	212	192	192	0
8	0	1	240	215	−215	0
8	0	2	136	135	135	0
8	0	3	159	174	−174	0
8	0	4	45	16	−16	0
8	0	5	9	26	26	0
8	0	6	11	5	−5	0
8	0	7	83	69	−69	0
8	0	8	63	63	63	0
8	0	9	39	34	−34	0
8	0	10	78	45	−45	0
8	0	11	72	53	−53	0
8	0	12	34	22	22	0
8	0	13	21	20	20	0
8	0	14	60	51	51	0
8	0	15	15	29	29	0
9	0	1	374	344	0	344
9	0	2	128	113	0	−113
9	0	3	180	182	0	182
9	0	4	193	182	0	−182
9	0	5	72	62	0	−62
9	0	6	225	230	0	−230
9	0	7	312	301	0	−301
9	0	8	45	12	0	12
9	0	9	343	336	0	−336
9	0	10	80	70	0	70
9	0	11	58	168	0	−168
9	0	12	22	33	0	33
9	0	13	20	31	0	31
9	0	14	68	65	0	65
9	0	15	72	68	0	68
10	0	0	58	57	−57	0
10	0	1	29	41	−41	0
10	0	2	149	149	−149	0
10	0	3	76	65	−65	0
10	0	4	139	137	−137	0
10	0	5	59	47	−47	0
10	0	6	11	32	32	0
10	0	7	56	32	32	0
10	0	8	154	138	138	0
10	0	9	122	113	−113	0
10	0	10	41	37	37	0
10	0	11	48	49	−49	0
10	0	12	19	15	15	0
10	0	13	18	29	−29	0
10	0	14	11	17	−17	0
11	0	1	83	74	0	74
11	0	2	133	136	0	136
11	0	3	52	62	0	62
11	0	4	187	188	0	188
11	0	5	111	97	0	−97
11	0	6	279	254	0	254
11	0	7	94	86	0	−86
11	0	8	96	78	0	78
11	0	9	61	66	0	−66
11	0	10	99	99	0	−99
11	0	11	26	14	0	−14
11	0	12	118	103	0	−103
12	0	0	56	46	46	0
12	0	1	14	14	−14	0
12	0	2	53	41	41	0
12	0	3	78	84	−84	0
12	0	4	8	6	−6	0
12	0	5	123	116	−116	0
12	0	6	11	28	28	0
12	0	7	35	32	−32	0
12	0	8	78	71	−71	0
12	0	9	72	67	67	0
12	0	10	18	5	−5	0
12	0	11	79	68	68	0
13	0	1	46	36	0	−36
13	0	2	67	55	0	55
13	0	3	27	25	0	−25
13	0	4	148	140	0	140
13	0	5	55	54	0	54
13	0	6	168	167	0	167
13	0	7	55	47	0	47
13	0	8	38	36	0	36
13	0	9	103	94	0	94
14	0	0	142	128	128	0
14	0	1	45	25	25	0
14	0	2	129	118	118	0
14	0	3	8	2	2	0
14	0	4	66	55	55	0
14	0	5	7	15	−15	0
14	0	6	92	85	−85	0
14	0	7	9	19	−19	0
15	0	1	98	90	0	−90
15	0	2	6	19	0	−19
15	0	3	53	51	0	−51
15	0	4	4	11	0	11
0	1	1	266	264	0	−264
0	1	2	190	241	241	0
0	1	3	448	354	0	354
0	1	4	635	652	−652	0
0	1	5	40	11	0	−11
0	1	6	276	270	−270	0
0	1	7	305	283	0	283
0	1	8	21	19	−19	0
0	1	9	6	27	0	27
0	1	10	48	23	23	0
0	1	11	34	55	0	−55
0	1	12	26	24	24	0
0	1	13	94	77	0	−77
0	1	14	35	48	−48	0
0	1	15	25	6	0	−6
0	1	16	22	21	−21	0
0	1	17	19	5	0	−5
0	1	18	47	51	−51	0
1	1	0	1352	1437	0	−1437
1	1	1	523	559	534	−167
1	1	2	694	744	274	−692
1	1	3	529	540	157	−516
1	1	4	389	338	306	143
1	1	5	443	431	−111	−416
1	1	6	98	107	96	45
1	1	7	248	237	−216	−98
1	1	8	323	322	92	309
1	1	9	146	137	−135	−21
1	1	10	272	269	−85	255
1	1	11	307	304	−100	287
1	1	12	139	132	0	132
1	1	13	188	175	−1	175
1	1	14	114	106	−82	−67
1	1	15	71	60	4	60
1	1	16	114	114	−2	−113
1	1	17	51	61	56	26
1	1	18	69	68	−15	−66
2	1	0	437	387	0	−387
2	1	1	366	341	231	251
2	1	2	322	332	306	129
2	1	3	129	151	−145	40
2	1	4	514	535	506	−173
2	1	5	315	331	−181	277
2	1	6	339	305	304	15
2	1	7	392	370	−354	107
2	1	8	205	191	187	38
2	1	9	95	78	−60	51
2	1	10	133	124	3	124
2	1	11	88	81	−29	−76
2	1	12	136	130	−128	24
2	1	13	92	77	−53	−56
2	1	14	48	59	−58	−10
2	1	15	94	95	90	−31
2	1	16	63	64	−62	−14
2	1	17	74	68	68	−3
2	1	18	12	18	−18	4
3	1	0	702	747	0	747
3	1	1	356	317	−35	−315
3	1	2	423	427	355	238
3	1	3	47	74	−2	−74
3	1	4	301	293	284	−71
3	1	5	39	30	−9	−29
3	1	6	156	160	147	64
3	1	7	79	92	74	55
3	1	8	151	151	−11	−151
3	1	9	112	120	−9	119
3	1	10	60	39	−36	−16
3	1	11	275	281	52	276
3	1	12	75	84	−77	−34
3	1	13	154	155	−49	147
3	1	14	89	84	−44	72
3	1	15	46	42	18	38
3	1	16	83	101	−49	89
3	1	17	16	31	−23	−21
3	1	18	11	16	9	13
4	1	0	80	68	0	−68
4	1	1	163	180	−179	20
4	1	2	366	337	−141	−306
4	1	3	147	147	146	−20
4	1	4	380	348	348	19
4	1	5	36	27	−23	−14
4	1	6	213	181	180	−18
4	1	7	235	216	199	−84
4	1	8	196	183	−33	180
4	1	9	245	214	203	−69
4	1	10	193	183	−131	128
4	1	11	25	27	27	5
4	1	12	85	54	−40	36
4	1	13	25	11	−12	3
4	1	14	59	40	−5	−40
4	1	15	87	77	−77	−4
4	1	16	47	47	30	−36
4	1	17	56	41	−40	6
5	1	0	611	589	0	589
5	1	1	297	285	−281	−47
5	1	2	462	431	74	425
5	1	3	102	101	−89	−49
5	1	4	205	206	102	−179
5	1	5	120	112	92	63
5	1	6	76	67	46	−49
5	1	7	175	170	95	−140
5	1	8	125	117	3	−117
5	1	9	153	144	138	−43
5	1	10	218	209	12	−209
5	1	11	182	155	18	−154
5	1	12	92	80	−19	−77
5	1	13	56	58	39	−44
5	1	14	65	60	−7	60
5	1	15	21	27	−26	9
5	1	16	65	63	−24	58
5	1	17	14	17	−17	2
6	1	0	95	119	0	−119
6	1	1	192	211	−175	−118
6	1	2	152	141	−129	−57
6	1	3	80	90	−18	−88
6	1	4	262	258	−249	−65
6	1	5	279	272	211	−171
6	1	6	134	109	−58	92
6	1	7	348	335	304	−142
6	1	8	119	120	−97	70
6	1	9	162	139	138	−13
6	1	10	91	85	72	46
6	1	11	135	120	90	79
6	1	12	160	145	145	−9
6	1	13	82	92	−36	85
6	1	14	63	46	42	−19
6	1	15	99	93	−88	30
6	1	16	33	39	31	−24
6	1	17	65	97	−97	−2
7	1	0	71	70	0	−70
7	1	1	319	291	−175	232
7	1	2	161	157	−101	−121
7	1	3	148	137	−36	133
7	1	4	101	102	−98	28
7	1	5	134	136	19	134
7	1	6	95	88	−64	−60
7	1	7	168	170	72	154
7	1	8	25	15	−15	−3
7	1	9	54	38	34	−17
7	1	10	88	78	−10	−78
7	1	11	119	102	43	−92
7	1	12	25	39	30	−25
7	1	13	72	75	19	−73
7	1	14	65	57	0	−57
7	1	15	35	39	11	−37
7	1	16	41	43	26	−35
8	1	0	115	122	0	122
8	1	1	152	155	151	−34
8	1	2	263	269	−259	72
8	1	3	175	173	−55	−164
8	1	4	452	467	−464	46
8	1	5	160	162	22	−161
8	1	6	456	465	−464	−29
8	1	7	176	165	−134	−95

TABLE 7. (*Continued.*)

h	k	l	$\|F_o\|$	$\|F_c\|$	A_c	B_c
8	1	8	160	138	−128	−52
8	1	9	163	140	−139	11
8	1	10	155	162	128	−99
8	1	11	98	96	−64	71
8	1	12	127	110	109	−15
8	1	13	80	68	13	67
8	1	14	109	114	114	13
8	1	15	46	48	28	38
9	1	0	32	23	0	−23
9	1	1	75	56	−29	−49
9	1	2	85	55	−55	−1
9	1	3	52	51	−32	−40
9	1	4	133	129	−66	110
9	1	5	161	160	22	−158
9	1	6	11	21	−21	−4
9	1	7	38	21	6	−20
9	1	8	103	90	−14	−89
9	1	9	69	48	14	46
9	1	10	35	26	19	19
9	1	11	92	75	16	74
9	1	12	21	20	−5	−19
9	1	13	38	46	9	45
9	1	14	31	43	18	−39
9	1	15	26	24	−9	22
10	1	0	145	127	0	127
10	1	1	192	184	184	7
10	1	2	149	153	99	117
10	1	3	86	91	81	42
10	1	4	115	105	101	29
10	1	5	158	155	−155	5
10	1	6	67	56	40	−39
10	1	7	207	192	−186	51
10	1	8	143	143	73	−123
10	1	9	169	162	−162	8
10	1	10	72	72	−24	−67
10	1	11	89	87	−87	−3
10	1	12	45	48	−41	−25
10	1	13	36	43	38	−21
10	1	14	16	34	−19	28
11	1	0	98	95	0	95
11	1	1	38	31	30	7
11	1	2	165	163	−55	154
11	1	3	98	92	12	92
11	1	4	58	58	−54	19
11	1	5	100	97	−2	97
11	1	6	78	80	−59	−54
11	1	7	13	25	2	25
11	1	8	46	43	2	−43
11	1	9	31	30	−1	30
11	1	10	20	29	4	−29
11	1	11	19	3	−3	0
11	1	12	14	26	26	−1
12	1	0	13	5	0	5
12	1	1	47	45	−8	45
12	1	2	95	98	96	16
12	1	3	63	60	26	54
12	1	4	120	126	126	7
12	1	5	91	92	15	91
12	1	6	160	167	166	−16
12	1	7	39	35	19	29
12	1	8	27	25	15	−20
12	1	9	42	36	34	13
12	1	10	86	85	−85	−3
12	1	11	40	58	28	−51
13	1	0	47	48	0	−48
13	1	1	83	75	67	33
13	1	2	56	56	−10	−56
13	1	3	56	50	36	35
13	1	4	45	54	−29	−46
13	1	5	60	72	−21	69
13	1	6	53	33	1	53
13	1	7	27	31	−31	1
13	1	8	74	74	−1	74
13	1	9	78	91	−38	−82
14	1	0	34	36	0	−36
14	1	1	81	80	−80	3
14	1	2	42	40	0	−40
14	1	3	55	49	−29	40
14	1	4	59	63	63	−3
14	1	5	58	59	46	37
14	1	6	56	52	52	−2
14	1	7	48	60	51	32
15	1	0	118	127	0	−127
15	1	1	39	48	46	−16
15	1	2	108	133	18	−132
0	2	0	1199	1183	−1183	0
0	2	1	457	497	0	−497
0	2	2	671	681	−681	0
0	2	3	252	239	0	−239
0	2	4	352	325	−325	0
0	2	5	149	147	0	147
0	2	6	78	67	−67	0
0	2	7	288	278	0	278
0	2	8	475	458	458	0
0	2	9	356	333	0	333
0	2	10	343	336	336	0
0	2	11	183	178	0	178
0	2	12	133	105	105	0
0	2	13	28	33	0	−33
0	2	14	87	74	−74	0
0	2	15	80	55	0	−55
0	2	16	103	91	−91	0
0	2	17	87	90	0	−90
1	2	0	55	39	39	0
1	2	1	207	212	104	−185
1	2	2	587	512	195	−473
1	2	3	115	110	83	−72
1	2	4	147	148	100	109
1	2	5	140	121	108	−53
1	2	6	243	241	−62	233
1	2	7	350	352	63	346
1	2	8	31	25	−22	−11
1	2	9	216	211	54	204
1	2	10	160	159	−38	−155
1	2	11	109	108	−71	82
1	2	12	63	66	1	−66
1	2	13	52	39	−39	4
1	2	14	35	52	−2	52
1	2	15	56	66	−28	−60
1	2	16	49	58	3	58
1	2	17	39	56	−22	−51
2	2	0	143	150	150	0
2	2	1	187	165	133	−97
2	2	2	353	370	88	−359
2	2	3	119	102	−101	7
2	2	4	281	242	−95	−222
2	2	5	303	281	−279	31
2	2	6	206	233	21	−222
2	2	7	210	210	−200	66
2	2	8	55	39	−12	−37
2	2	9	141	128	89	92
2	2	10	142	139	82	112
2	2	11	336	347	347	11
2	2	12	153	145	−32	141
2	2	13	159	161	160	13
2	2	14	91	105	−14	104
2	2	15	22	39	−12	−37
2	2	16	19	28	16	22
2	2	17	15	19	3	−19
3	2	0	73	116	−116	0
3	2	1	400	367	98	354
3	2	2	154	145	−145	6
3	2	3	207	185	166	−82
3	2	4	479	460	122	−444
3	2	5	169	145	145	5
3	2	6	246	240	−25	−238
3	2	7	189	170	98	139
3	2	8	167	147	117	−88
3	2	9	127	118	−67	97
3	2	10	120	120	78	91
3	2	11	39	64	−47	−44
3	2	12	119	109	47	99
3	2	13	87	94	−76	−55
3	2	14	26	27	−13	24
3	2	15	81	78	−39	−67
3	2	16	20	18	−17	5
3	2	17	15	11	8	−8
4	2	0	594	518	518	0
4	2	1	129	104	50	91
4	2	2	183	157	117	−104
4	2	3	156	132	125	43
4	2	4	168	173	87	−149
4	2	5	132	115	33	−110
4	2	6	100	79	−27	−74
4	2	7	235	223	−204	−90
4	2	8	114	115	−113	−23
4	2	9	189	173	53	−164
4	2	10	159	147	−142	39
4	2	11	32	42	31	−29
4	2	12	96	96	21	94
4	2	13	29	30	6	30
4	2	14	105	98	94	28
4	2	15	25	60	−35	54
4	2	16	21	88	22	33
5	2	0	202	221	−221	0
5	2	1	185	176	−152	88
5	2	2	313	274	−118	248
5	2	3	189	187	10	−187
5	2	4	58	66	−64	14
5	2	5	201	193	−76	−177
5	2	6	356	327	172	−278
5	2	7	210	193	−38	−185
5	2	8	138	131	124	42
5	2	9	108	98	−35	−91
5	2	10	190	170	133	106
5	2	11	31	46	46	−3
5	2	12	29	38	−13	36
5	2	13	28	27	25	10
5	2	14	73	62	−48	−38
5	2	15	116	98	22	96
5	2	16	52	66	−58	−33
6	2	0	11	8	8	0
6	2	1	214	218	−10	218
6	2	2	180	170	145	89
6	2	3	179	190	186	37
6	2	4	139	135	133	23
6	2	5	103	94	92	19
6	2	6	51	58	14	56
6	2	7	196	188	143	−122
6	2	8	85	95	−95	−9
6	2	9	181	163	−103	−126
6	2	10	189	182	−181	9
6	2	11	183	155	−139	−69
6	2	12	31	61	−31	−53
6	2	13	122	105	−103	−20
6	2	14	26	5	−5	2
6	2	15	22	23	−12	20
6	2	16	18	41	−40	−10
7	2	0	95	94	−94	0
7	2	1	78	70	−70	3
7	2	2	282	284	−42	280
7	2	3	353	347	−304	166
7	2	4	329	355	−85	345
7	2	5	215	197	−186	−64
7	2	6	208	236	43	232
7	2	7	216	194	−168	−96
7	2	8	93	82	52	64
7	2	9	133	109	56	−93
8	2	0	300	317	−317	0
8	2	1	32	49	18	46
8	2	2	125	137	−135	23
8	2	3	118	131	−129	24
8	2	4	63	64	11	63
8	2	5	9	9	9	−2
8	2	6	106	89	89	−2
8	2	7	99	101	98	−24
8	2	8	39	51	−22	46
8	2	9	22	22	22	4
9	2	0	308	275	275	0
9	2	1	270	262	−18	−262
9	2	2	145	127	127	6
9	2	3	116	110	−107	−25
9	2	4	103	110	60	93
9	2	5	220	206	−126	162
9	2	6	227	215	−113	183
9	2	7	142	123	−30	120
9	2	8	143	134	−133	14
9	2	9	147	138	6	138
10	2	0	201	195	195	0
10	2	1	93	85	−60	61
10	2	2	108	107	104	26
10	2	3	103	100	−76	65
10	2	4	56	62	57	25
10	2	5	46	47	−31	−35
10	2	6	91	88	−73	49
10	2	7	32	24	−11	−21
10	2	8	42	40	−39	9
10	2	9	106	88	77	−42
11	2	0	91	91	91	0
11	2	1	39	34	34	−5
11	2	2	183	181	78	−163
11	2	3	113	113	113	−1
11	2	4	120	123	16	−122
11	2	5	80	86	68	53
11	2	6	112	109	−47	−99
11	2	7	71	57	47	33
11	2	8	98	95	−94	−10
11	2	9	9	17	−10	−13

XUM

TABLE 7. (*Continued.*)

h	k	l	$\|F_o\|$	$\|F_c\|$	A_c	B_c
12	2	0	73	68	68	0
12	2	1	49	48	17	−45
12	2	2	76	73	47	56
12	2	3	95	79	69	−38
12	2	4	107	103	−65	79
12	2	5	39	39	39	7
12	2	6	73	77	−42	64
12	2	7	11	4	−4	2
12	2	8	33	36	36	−5
12	2	9	67	52	−44	28
13	2	0	39	41	−41	0
13	2	1	86	72	31	65
13	2	2	16	26	−6	−25
13	2	3	89	82	81	−10
13	2	4	63	68	2	−67
13	2	5	69	115	85	−78
13	2	6	63	62	6	−62
13	2	7	49	54	38	−38
13	2	8	26	28	23	−17
14	2	0	68	50	−50	0
14	2	1	100	89	28	−84
14	2	2	78	71	−70	9
14	2	3	51	50	30	−40
14	2	4	33	37	−28	24
14	2	5	31	33	25	21
14	2	6	28	38	37	−8
0	3	1	11	5	0	−5
0	3	2	96	98	−98	0
0	3	3	178	180	0	−180
0	3	4	415	415	415	0
0	3	5	53	37	0	−37
0	3	6	314	317	317	0
0	3	7	15	47	0	−47
0	3	8	48	54	54	0
0	3	9	79	73	0	−73
0	3	10	170	169	−169	0
0	3	11	14	8	0	−8
9	3	12	114	98	−98	0
0	3	13	14	17	0	−17
0	3	14	13	11	−11	0
0	3	15	12	16	0	16
0	3	16	9	20	20	0
0	3	17	35	58	0	58
1	3	0	316	324	0	324
1	3	1	426	394	−393	32
1	3	2	320	344	−287	190
1	3	3	235	239	−224	83
1	3	4	249	247	−240	58
1	3	5	236	223	22	222
1	3	6	274	270	−267	38
1	3	7	216	222	218	45
1	3	8	142	150	−106	−106
1	3	9	310	309	309	−2
1	3	10	88	97	59	−77
1	3	11	218	232	174	−154
1	3	12	128	115	112	−25
1	3	13	40	62	−20	−59
1	3	14	113	93	91	22
1	3	15	54	59	−59	−2
1	3	16	9	24	17	17
1	3	17	32	62	−60	−16
2	3	0	259	247	0	247
2	3	1	182	182	−121	−136
2	3	2	133	129	−107	−72
2	3	3	279	267	−30	−266
2	3	4	167	169	−164	−39
2	3	5	214	212	71	−199
2	3	6	34	29	−25	14
2	3	7	342	337	298	−158
2	3	8	99	103	−99	31
2	3	9	183	170	170	−2
2	3	10	54	38	−38	8
2	3	11	41	54	47	26
2	3	12	14	37	−3	−37
2	3	13	59	68	−14	67
2	3	14	53	63	30	−56
2	3	15	82	89	−71	54
2	3	16	9	26	16	−20
3	3	0	345	341	0	−341
3	3	1	142	116	69	−93
3	3	2	303	272	−214	−167
3	3	3	120	118	63	−99
3	3	4	242	244	−242	31
3	3	5	82	103	−77	−69
3	3	6	194	202	−202	−3
3	3	7	72	62	−60	17
3	3	8	151	164	−120	12
3	3	9	138	136	−84	−106
3	3	10	107	101	98	25
3	3	11	96	113	−42	−105
3	3	12	131	146	145	17
3	3	13	42	41	40	−9
3	3	14	88	106	94	−48
3	3	15	45	48	26	41
3	3	16	45	63	5	−63
4	3	0	334	313	0	313
4	3	1	79	70	14	−68
4	3	2	248	221	68	211
4	3	3	174	174	−165	54
4	3	4	166	167	−167	−1
4	3	5	79	65	3	−65
4	3	6	236	236	−193	−137
4	3	7	46	60	2	60
4	3	8	103	107	30	−102
4	3	9	91	76	48	59
4	3	10	167	168	107	−130
4	3	11	67	68	2	68
4	3	12	94	75	70	−25
4	3	13	26	46	0	46
4	3	14	12	16	−16	3
4	3	15	9	20	7	19
4	3	16	7	32	−11	30
5	3	0	194	185	0	−185
5	3	1	263	259	259	−10
5	3	2	115	99	42	−90
5	3	3	159	170	92	−143
5	3	4	81	64	−43	−48
5	3	5	103	100	33	−94
5	3	6	39	54	−48	25
5	3	7	160	159	−158	12
5	3	8	31	47	−46	11
5	3	9	207	207	−199	55
5	3	10	91	82	−26	88
5	3	11	156	165	−119	114
5	3	12	14	15	15	1
5	3	13	71	80	15	79
5	3	14	12	28	−14	−24
5	3	15	38	45	40	21
6	3	0	122	100	0	100
6	3	1	163	168	35	165
6	3	2	216	215	61	206
6	3	3	212	214	2	214
6	3	4	49	32	32	−3
6	3	5	201	218	−131	174
6	3	6	113	109	−88	−65
6	3	7	159	155	−100	118
6	3	8	170	169	21	−168
6	3	9	88	84	−80	−25
6	3	10	65	70	43	−55
6	3	11	14	53	−5	−53
6	3	12	13	21	−12	−18
6	3	13	61	73	7	−72
6	3	14	42	50	0	50
6	3	15	58	84	59	−60
7	3	0	269	283	0	283
7	3	1	108	110	97	−51
7	3	2	138	147	103	105
7	3	3	81	83	63	−55
7	3	4	134	145	145	−6
7	3	5	94	101	43	−92
7	3	6	119	114	77	−84
7	3	7	120	115	−8	−115
7	3	8	86	98	91	−36
7	3	9	88	85	−78	32
7	3	10	34	38	−9	−37
7	3	11	49	71	−39	59
7	3	12	41	57	−57	−7
7	3	13	45	53	−45	27
7	3	14	39	57	−33	46
8	3	0	154	157	0	−157
8	3	1	159	154	−60	142
8	3	2	163	180	93	−154
8	3	3	242	238	52	232
8	3	4	146	151	149	18
8	3	5	260	280	29	278
8	3	6	189	203	197	49
8	3	7	89	82	2	82
8	3	8	92	86	38	77
8	3	9	34	34	32	12
8	3	10	67	80	−26	76
8	3	11	74	102	10	−102
8	3	12	35	38	−29	24
8	3	13	68	99	20	−97
8	3	14	45	22	−22	−1
9	3	0	47	49	0	49
9	3	1	60	60	20	57
9	3	2	55	58	−13	56
9	3	3	165	171	53	162
9	3	4	53	64	−25	−58
9	3	5	108	119	−18	118
9	3	6	44	42	36	−21
9	3	7	58	51	−6	51
9	3	8	11	21	21	−2
9	3	9	53	44	−3	−44
9	3	10	12	33	17	−28
9	3	11	59	67	−18	−65
9	3	12	9	19	−18	4
9	3	13	28	73	−10	−73
10	3	0	203	220	0	−220
10	3	1	67	75	−30	−68
10	3	2	185	195	−95	−170
10	3	3	32	42	17	−39
10	3	4	47	64	−61	−18
10	3	5	96	108	87	−64
10	3	6	88	85	−30	79
10	3	7	53	47	32	−35
10	3	8	140	163	−17	162
10	3	9	28	17	12	−11
10	3	10	56	79	−12	78
10	3	11	8	27	21	18
11	3	0	113	125	0	−125
11	3	1	38	40	13	38
11	3	2	94	108	30	−103
11	3	3	9	9	−8	4
11	3	4	59	58	58	7
11	3	5	34	37	−21	31
11	3	6	86	91	75	53
11	3	7	45	55	−54	10
11	3	8	38	36	22	29
11	3	9	7	19	−1	−19
11	3	10	8	41	−23	34
12	3	0	11	7	0	−7
12	3	1	76	75	56	−49
12	3	2	21	30	−28	10
12	3	3	106	126	14	−126
12	3	4	28	33	−29	−16
12	3	5	96	115	−34	−109
12	3	6	42	40	−36	16
12	3	7	40	51	−38	−35
12	3	8	47	3	0	−3
13	3	0	9	44	0	−44
13	3	1	71	76	−71	−27
13	3	2	33	32	25	−19
13	3	3	35	48	−47	−10
13	3	4	52	69	60	33
13	3	5	5	19	1	−19
13	3	6	6	15	11	10
14	3	0	51	85	0	85
14	3	1	36	49	47	−13
14	3	2	45	63	38	50
14	3	3	28	43	0	−43
0	4	0	342	340	340	0
0	4	1	347	337	0	337
0	4	2	101	86	86	0
0	4	3	209	197	0	197
0	4	4	99	118	−118	0
0	4	5	108	118	0	−118
0	4	6	9	4	4	0
0	4	7	170	167	0	−167
0	4	8	78	72	72	0
0	4	9	297	290	0	−290
0	4	10	28	34	34	0
0	4	11	141	126	0	−126
0	4	12	26	40	−40	0
0	4	13	24	3	0	3
0	4	14	20	21	−21	0
0	4	15	56	62	0	62
1	4	0	179	182	−182	0
1	4	1	269	257	−16	257
1	4	2	192	204	−117	−167
1	4	3	49	46	43	14
1	4	4	252	273	−110	−250
1	4	5	87	98	−19	−96
1	4	6	148	164	127	−104
1	4	7	132	148	−13	−147
1	4	8	51	53	51	14
1	4	9	116	113	−68	−90
1	4	10	110	111	98	49
1	4	11	25	62	−5	−62
1	4	12	47	46	−4	46

TABLE 7. (*Continued.*)

h	k	l	$\|F_o\|$	$\|F_c\|$	A_c	B_c
1	4	13	21	47	−24	41
1	4	14	19	44	−18	40
1	4	15	14	35	6	35
2	4	0	114	109	−109	0
2	4	1	31	31	24	21
2	4	2	281	278	−83	265
2	4	3	54	43	20	−38
2	4	4	174	183	−77	166
2	4	5	58	87	−82	27
2	4	6	179	173	27	171
2	4	7	121	141	−136	−38
2	4	8	111	106	104	20
2	4	9	69	56	−55	−10
2	4	10	80	88	62	−63
2	4	11	25	39	−32	−23
2	4	12	119	125	6	−125
2	4	13	20	9	−3	8
2	4	14	78	78	−15	−77
2	4	15	13	14	14	1
3	4	0	28	37	37	0
3	4	1	267	255	−55	249
3	4	2	29	27	−19	19
3	4	3	181	189	−188	18
3	4	4	128	137	−18	136
3	4	5	174	183	−94	−157
3	4	6	87	81	31	75
3	4	7	165	159	−97	−126
3	4	8	33	28	21	20
3	4	9	93	89	71	−53
3	4	10	27	28	−16	−23
3	4	11	82	73	40	−61
3	4	12	25	37	−23	−29
3	4	13	74	86	80	−31
3	4	14	19	27	−27	4
3	4	15	42	53	43	30
4	4	0	182	176	−176	0
4	4	1	138	125	17	−124
4	4	2	49	48	−48	4
4	4	3	132	117	−111	−37
4	4	4	121	122	110	53
4	4	5	182	197	−180	80
4	4	6	29	30	17	−24
4	4	7	165	162	−116	113
4	4	8	52	59	−38	45
4	4	9	145	131	−5	131
4	4	10	29	33	−25	−21
4	4	11	96	94	79	51
4	4	12	26	18	4	−17
4	4	13	71	84	70	−47
4	4	14	19	29	−27	−11
5	4	0	131	122	122	0
5	4	1	107	105	0	105
5	4	2	175	169	103	133
5	4	3	107	101	−15	100
5	4	4	143	157	16	156
5	4	5	28	36	−25	25
5	4	6	158	150	−114	99
5	4	7	51	55	52	18
5	4	8	95	91	−91	−8
5	4	9	22	19	14	−14
5	4	10	98	88	−81	−36
5	4	11	26	38	15	−35
5	4	12	24	16	14	−7
5	4	13	21	33	13	−31
5	4	14	16	58	43	−39
6	4	0	56	47	47	0
6	4	1	142	130	−67	−112
6	4	2	146	140	52	−130
6	4	3	86	83	−83	−7
6	4	4	151	151	83	−126
6	4	5	120	110	−102	−43
6	4	6	73	58	−23	−53
6	4	7	53	51	−27	43
6	4	8	121	120	−116	−29
6	4	9	86	69	39	56
6	4	10	91	62	−49	38
6	4	11	26	91	78	48
6	4	12	24	53	16	51
6	4	13	20	53	46	27
7	4	0	88	91	91	0
7	4	1	161	148	103	−107
7	4	2	82	80	60	54
7	4	3	192	180	178	−26
7	4	4	35	36	36	−4
7	4	5	179	188	171	77
7	4	6	61	57	−33	−46
7	4	7	119	100	92	39
7	4	8	73	69	−63	−28
7	4	9	11	23	−22	5
8	4	0	182	176	176	0
8	4	1	66	60	−5	59
8	4	2	143	151	150	−5
8	4	3	58	44	44	3
8	4	4	8	13	−13	−2
8	4	5	99	108	107	−15
8	4	6	63	59	−55	22
8	4	7	89	87	60	−64
8	4	8	72	75	−73	−19
8	4	9	54	41	−4	−41
9	4	0	176	171	−171	0
9	4	1	51	45	0	−45
9	4	2	159	129	−129	4
9	4	3	105	102	101	−17
9	4	4	34	30	−29	−7
9	4	5	66	62	62	−6
9	4	6	83	75	68	−32
9	4	7	32	26	17	−19
9	4	8	115	117	117	0
9	4	9	8	18	−6	−17
10	4	0	48	54	−34	0
10	4	1	95	70	45	−54
10	4	2	88	84	−73	41
10	4	3	91	89	70	−55
10	4	4	80	81	−54	61
10	4	5	125	118	118	10
10	4	6	8	7	−1	7
10	4	7	78	82	68	46
10	4	8	54	57	57	−4
10	4	9	60	49	−36	32
11	4	0	56	59	−59	0
11	4	1	92	71	−28	−65
11	4	2	8	13	−9	−9
11	4	3	100	105	−98	−37
11	4	4	16	20	−20	4
11	4	5	75	72	−71	−10
11	4	6	51	47	35	32
11	4	7	54	56	−41	38
11	4	8	29	37	36	7
12	4	0	71	69	−69	0
12	4	1	9	2	−2	0
12	4	2	61	65	−61	−21
12	4	3	27	27	25	10
12	4	4	51	51	−7	−51
12	4	5	5	12	3	12
12	4	6	45	50	29	−41
13	4	0	67	65	65	0
13	4	1	6	15	−10	−10
13	4	2	42	46	16	−43
0	5	1	140	120	0	−120
0	5	2	143	128	−128	0
0	5	3	167	158	0	−158
0	5	4	153	149	−149	0
0	5	5	141	132	0	−132
0	5	6	95	89	−89	0
0	5	7	13	4	0	−4
0	5	8	11	18	18	0
0	5	9	59	66	0	66
0	5	10	26	13	13	0
0	5	11	32	50	0	50
0	5	12	56	68	68	0
0	5	13	52	54	0	54
1	5	0	102	113	0	−113
1	5	1	160	152	149	26
1	5	2	163	160	160	13
1	5	3	89	83	56	−62
1	5	4	125	128	120	45
1	5	5	52	65	−57	31
1	5	6	93	97	96	−13
1	5	7	67	84	−83	8
1	5	8	93	93	17	−92
1	5	9	94	90	−88	17
1	5	10	24	39	−29	−26
1	5	11	21	50	−50	1
1	5	12	19	46	−41	21
1	5	13	14	13	3	12
2	5	0	154	139	0	139
2	5	1	153	145	142	28
2	5	2	170	178	−35	174
2	5	3	47	46	−23	40
2	5	4	22	13	−13	2
2	5	5	129	129	−113	63
2	5	6	112	119	24	−116
2	5	7	87	94	−59	73
2	5	8	120	116	9	−115
2	5	9	69	62	−59	19
2	5	10	44	62	21	−58
2	5	11	20	39	−38	−9
2	5	12	18	3	1	−2
2	5	13	14	39	−33	−21
3	5	0	140	145	0	145
3	5	1	100	83	−83	−10
3	5	2	101	99	97	17
3	5	3	74	73	−56	47
3	5	4	56	60	58	12
3	5	5	121	123	61	106
3	5	6	49	36	−11	−34
3	5	7	115	118	77	90
3	5	8	11	16	−15	−5
3	5	9	91	80	79	8
3	5	10	24	33	−26	−20
3	5	11	21	44	33	−29
3	5	12	18	23	−23	−1
3	5	13	13	44	−37	−24
4	5	0	18	21	0	21
4	5	1	141	139	114	80
4	5	2	44	42	37	−21
4	5	3	116	105	22	103
4	5	4	52	56	55	−9
4	5	5	100	101	−35	94
4	5	6	33	35	35	−3
4	5	7	31	36	−34	−11
4	5	8	9	16	−13	9
4	5	9	69	55	−11	−54
4	5	10	25	40	−21	34
4	5	11	44	80	−58	−56
4	5	12	56	17	−16	−4
5	5	0	41	48	0	48
5	5	1	113	100	−100	−5
5	5	2	89	85	−83	19
5	5	3	62	63	−9	63
5	5	4	105	101	−74	−69
5	5	5	87	77	20	74
5	5	6	78	65	−63	17
5	5	7	83	74	62	41
5	5	8	69	71	1	71
5	5	9	79	64	54	−34
5	5	10	72	58	54	21
5	5	11	20	65	21	−61
5	5	12	15	53	48	−22
6	5	0	116	95	0	−95
6	5	1	34	31	4	−31
6	5	2	136	126	73	−103
6	5	3	29	37	36	5
6	5	4	53	54	51	−19
6	5	5	39	52	44	−28
6	5	6	61	61	8	61
6	5	7	55	49	10	−48
6	5	8	102	98	5	98
6	5	9	25	14	−14	3
6	5	10	22	43	−8	43
6	5	11	18	23	4	23
7	5	0	99	89	0	−89
7	5	1	59	59	51	39
7	5	2	138	108	−74	−78
7	5	3	40	41	34	23
7	5	4	89	90	−87	−23
7	5	5	151	30	−28	12
7	5	6	51	46	−27	37
7	5	7	63	71	−70	7
7	5	8	71	76	−21	73
7	5	9	69	56	−56	−2
8	5	0	12	13	0	13
8	5	1	73	61	−41	−46
8	5	2	34	43	22	37
8	5	3	138	121	4	−121
8	5	4	7	4	−2	4
8	5	5	91	125	23	−123
8	5	6	27	34	−34	−3
8	5	7	60	55	−7	−55
8	5	8	31	23	−11	−20
8	5	9	7	10	−10	−3
9	5	0	53	57	0	−57
9	5	1	12	21	15	−15
9	5	2	66	63	61	−18
9	5	3	58	48	−16	−45
9	5	4	96	98	96	20

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TABLE 7. (*Continued.*)

h	k	l	$\|F_o\|$	$\|F_c\|$	A_c	B_c
9	5	5	42	89	−5	−88
9	5	6	78	75	70	26
9	5	7	54	59	−26	−53
9	5	8	18	18	17	−5
10	5	0	65	73	0	73
10	5	1	66	55	−50	22
10	5	2	56	49	10	48
10	5	3	32	36	−23	28
10	5	4	35	34	23	26
10	5	5	5	34	−11	32
10	5	6	31	37	25	−28
10	5	7	18	36	15	32
11	5	1	60	49	−49	−2
11	5	2	42	38	12	36
11	5	3	45	43	−27	−33
11	5	4	19	27	16	22
0	6	0	56	49	49	0
0	6	1	142	128	0	−128
0	6	2	20	28	28	0
0	6	3	94	80	0	−80
0	6	4	8	5	5	0
0	6	5	20	27	0	27
0	6	6	44	46	−46	0
0	6	7	92	91	0	91
0	6	8	33	30	−30	0
0	6	9	103	92	0	92
0	6	10	18	18	−18	0
0	6	11	39	59	0	59
1	6	0	94	90	90	0
1	6	1	29	55	−43	−34
1	6	2	133	120	120	0
1	6	3	71	73	−72	−14
1	6	4	54	52	19	48
1	6	5	59	62	−62	2
1	6	6	85	95	−61	72
1	6	7	86	24	−5	24
1	6	8	94	93	−87	31
1	6	9	55	57	43	38
1	6	10	15	66	−60	−27
1	6	11	9	46	41	22
2	6	0	60	64	64	0
2	6	1	52	46	38	26
2	6	2	87	101	34	−95
2	6	3	91	93	90	21
2	6	4	86	80	4	−80
2	6	5	36	38	37	−9
2	6	6	66	55	−23	−51
2	6	7	27	35	29	−21
2	6	8	26	25	−24	−7
2	6	9	28	25	21	−14
2	6	10	14	41	−15	38
3	6	0	80	70	70	0
3	6	1	81	74	59	−45
3	6	2	46	54	51	16
3	6	3	69	75	67	−32
3	6	4	20	20	19	−6
3	6	5	74	78	77	−11
3	6	6	55	65	−64	−13
3	6	7	32	45	31	33
3	6	8	65	67	−67	−2
3	6	9	60	55	−26	48
3	6	10	14	34	−33	6
4	6	0	16	27	−27	0
4	6	1	92	72	32	64
4	6	2	47	35	−2	35
4	6	3	86	83	74	36
4	6	4	49	45	−20	40
4	6	5	66	66	57	−33
4	6	6	41	49	25	42
4	6	7	53	76	19	−73
4	6	8	7	18	15	10
4	6	9	68	70	6	−69
5	6	0	15	18	−18	0
5	6	1	79	47	2	−47
5	6	2	36	36	−35	6
5	6	3	81	82	65	−50
5	6	4	20	31	−4	−31
5	6	5	42	41	36	−19
5	6	6	63	71	38	−60
5	6	7	59	13	3	13
5	6	8	44	48	36	−31
5	6	9	52	46	−26	38
6	6	0	62	65	−65	0
6	6	1	16	10	10	0
6	6	2	94	99	−48	86
6	6	3	7	9	−8	−5
6	6	4	94	100	7	100
6	6	5	41	41	31	28
6	6	6	73	70	21	66
6	6	7	15	21	10	19
6	6	8	22	29	27	11
7	6	0	73	70	70	0
7	6	1	31	31	−26	−18
7	6	2	31	30	−29	6
7	6	3	80	69	−69	8
7	6	4	40	36	−28	−22
7	6	5	58	52	−52	2
7	6	6	33	39	26	−29
7	6	7	33	39	−39	−2
8	6	0	60	51	−51	0
8	6	1	85	78	−30	−73
8	6	2	61	49	−42	−26
8	6	3	47	49	−35	−34
8	6	4	29	26	9	−24
8	6	5	31	36	−31	18
9	6	0	72	70	70	0
9	6	1	6	25	2	25
9	6	2	51	48	42	−23
0	7	1	53	49	0	49
0	7	2	44	40	−40	0
0	7	3	102	93	0	93
0	7	4	6	2	−2	0
0	7	5	98	103	0	103
0	7	6	35	38	38	0
1	7	0	40	38	0	−38
1	7	1	19	23	−7	−22
1	7	2	44	43	−40	−17
1	7	3	48	40	−20	−34
1	7	4	45	40	−36	18
1	7	5	5	6	0	−6
1	7	6	32	37	−33	16
2	7	0	83	91	0	−91
2	7	1	22	24	20	−14
2	7	2	93	96	−10	−95
2	7	3	6	7	−5	−5
2	7	4	34	38	1	−38
2	7	5	12	13	−12	−6
2	7	6	40	58	17	56
3	7	0	34	4	0	4
3	7	1	62	60	45	−40
3	7	2	7	10	9	5
3	7	3	61	57	31	−48
3	7	4	15	20	20	4
3	7	5	32	30	−25	−15
4	7	0	27	28	0	−28
4	7	1	29	26	−4	−25
4	7	2	45	34	30	−17
4	7	3	66	70	−26	−65
4	7	4	26	26	12	−23
4	7	5	33	56	−17	−54
5	7	0	26	27	0	27
5	7	1	7	2	−2	0
5	7	2	59	71	69	19

Table 2 gives the anisotropic thermal parameters (in Å²). These are the components of Cruickshank's anisotropic thermal motion tensor.[8]

Table 3 gives the standard deviations and σ_{rms} for the atomic co-ordinates. The values were found from the standard least-squares formulæ.[9]

For Table 4 the deviations were calculated from the formulæ given by Cruickshank and Robertson.[10]

Table 5 gives the standard deviations of the anisotropic thermal parameters.

Table 6 gives some of the smaller Van der Waals contacts.

Table 7 gives $|F_o|$, $|F_c|$, A_c, and B_c.

Discussion.—In Table 8 the bond lengths obtained in the present analysis are compared with standard lengths given in " Interatomic Distances." [11] It will be seen that the agreement is everywhere good except for the C=N bond, which is not significantly different from a carbon–nitrogen triple bond. The same feature was observed in the two previous studies on vinylideneamines.[1,2]

The angle C3=C4=N1 differs significantly from 180° ($\Delta/\sigma = 6{\cdot}0$) but the direction of displacement of the nitrogen atom is perpendicular to the plane S1–C4–S2. Such a

[8] Cruickshank, *Acta Cryst.*, 1956, **9**, 747.
[9] Whittaker and Robinson, " Calculus of Observations," Chapter IX, Blackie and Sons, London, 1940.
[10] Cruickshank and Robertson, *Acta Cryst.*, 1953, **6**, 698.
[11] Interatomic Distances " (L. E. Sutton), *Chem. Soc. Special Publ.* No. 11, London, 1958.

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distortion preserves the *mm* symmetry of the π-bond in C4=N1, and thus might occur particularly easily.

In Table 9 the present molecular dimensions are compared with the analogous ones obtained by Wheatley for $(CH_3{\cdot}SO_2)_2C{=}C{=}NMe$. Some differences in bond angles occur but these, with the exception of C4=N1–C5, are small and are probably attributable to

TABLE 8. *Bond lengths* (Å) *and angles in* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$ *compared with standard values taken from "Interatomic Distances."* [10]

Bond	Length in $(CH_3{\cdot}SO_2)_2C{=}C{=}NEt$	Length in standard	Standard source
S1–O1	1·441	1·43	Sulphones
S2–O2	1·440	1·43	Sulphones
S1–O3	1·433	1·43	Sulphones
S2–O4	1·432	1·43	Sulphones
S1–C1	1·773	1·80	S-methyl
S2–C2	1·772	1·80	S-methyl
S1–C3	1·739	1·73	S–C heterocyclic
S2–C3	1·741	1·73	S–C heterocyclic
N1–C4	1·165	—	Not enough data
N1–C5	1·465	1·475	N–C normal
C3–C4	1·356	1·337	C–C normal
C5–C6	1·532	1·541	C–C normal

Angle	Size in $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$	Size in standard
S1–C3–S2	121·5°	120·0°
S1–C3–C4	121·8	120·0
S2–C3–C4	116·6	120·0
N1–C4–C3	173·4	180·0
N1–C5–C6	111·2	109·5
O1–S1–O3	118·8	109·5
O1–S1–C1	108·6	109·5
O1–S1–C3	107·7	109·5
O2–S2–O4	118·7	109·5
O2–S2–C2	108·2	109·5
O2–S2–C3	106·0	109·5
O3–S1–C1	107·7	109·5
O3–S1–C3	107·2	109·5
O4–S2–C2	108·6	109·5
O4–S2–C3	108·0	109·5
C1–S1–C3	106·2	109·5
C2–S2–C3	106·7	109·5
C4–N1–C5	144·5	120·0

TABLE 9. *Comparison of the bond lengths* (Å) *and angles in* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}C_2H_5$ *with corresponding values in* $(CH_3{\cdot}SO_2)_2C{=}C{=}N{\cdot}CH_3$.

Bond	Length in NEt compound	Length in NMe compound	Δ/σ
S1–O1	1·441	1·431	1·4
S2–O2	1·440	1·431	0·9
S1–O3	1·433	1·435	0·3
S2–O4	1·432	1·435	0·3
S1–C1	1·773	1·770	0·3
S2–C2	1·772	1·770	0·1
S1–C3	1·739	1·726	1·3
S2–C3	1·741	1·726	1·4
N1–C4	1·165	1·154	0·8
N1–C5	1·465	1·426	2·4
C3–C4	1·356	1·342	0·9
C5–C6	1 532	—	—
Distance			
S1–S2	3·03	3·03	—

Angle	Size in NEt compound	Size in NMe compound	Δ/σ
S1–C3–S2	121·5°	122·6°	0·7
S1–C3–C4	121·8	118·7	3·9
S2–C3–C4	116·6	118·7	2·6
N1–C4–C3	173·4	180·0	6·0
N1–C5–C6	111·2	—	—
O1–S1–O3	118·8	118·4	0·8
O1–S1–C1	108·6	108·7	0·2
O1–S1–C3	107·7	107·3	0·8
O2–S2–O4	118·7	118·4	0·6
O2–S2–C2	108·2	108·7	0·8
O2–S2–C3	106·0	107·3	2·6
O3–S1–C1	107·7	106·7	2·0
O3–S1–C3	107·2	108·3	2·2
O4–S2–C2	108·6	106·7	3·2
O4–S2–C3	108·0	108·3	0·6
C1–S1–C3	106·2	106·7	1·0
C2–S2–C3	106·7	106·7	—
C4–N1–C5	144·5	180·0	31·0

packing requirements. The lengths of the C3=C4, C4=N1, and N1–C5 bonds are all found to be slightly, though not significantly, greater than those found by Wheatley (Δ/σ values are 0·9, 0·8, and 2·4 respectively). It is interesting that the N1–C5 bond is significantly longer than was found by Bullough and Wheatley for $CH_3{\cdot}SO_2{\cdot}C(SO_2{\cdot}Ph){=}C{=}NMe$ (Δ/σ = 5·2).

There is no significant difference between the length of the N1–C5 bond found here (1·465 Å) and the standard single bond value (1·475 Å). Thus the length of the N1–C5 bond is consistent with the absence of hyperconjugation.

The most noticeable feature of the present analysis is the value found for the angle C4=N1–C5. The angle between the valencies of the nitrogen atom is no longer 180°,

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nor has the angle dropped to 120°, but an intermediate value of 144° is adopted. These values indicate that the methyl group, attached to the nitrogen atom in *N*-methylvinylideneamines, brings about complete delocalisation of the lone pair of electrons on the nitrogen, while a similarly substituted ethyl group cannot do so. By analogy, a carbanion of the type RR′C=C=C̄–Me ought to have a linear C=C–Me angle.

In view of these results it seems reasonable to classify the *N*-methylvinylideneamines investigated [1,2] as examples of hyperconjugation in molecules in the ground state. However, it cannot be assumed that hyperconjugation is the only factor affecting linearity. In the *N*-ethylvinylideneamine the shortness of the N1=C4 bond, and the intermediate value adopted by the C4=N1–C5 angle could be ascribed either to the reduced hyperconjugation of the ethyl group or to the electron-attracting power of the sulphonyl groups. A more thorough examination of the effects of electronegativity is required to establish the relative importance of hyperconjugation and electronegativity.

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Department of Inorganic and Structural Chemistry,
The University, Leeds, 2.
[Present address: Monsanto Research S.A.,
Binzstrasse 39, Zurich 3/45, Switzerland. [*Received, January 12th*, 1961.]

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547. *A Coloured Maleimide and its Interaction with Cysteine.*

By G. D. Clark-Walker and H. C. Robinson.

The preparation of *N*-2,4-dinitroanilinomaleimide is described. Cyclization of the cysteine addition compound of this maleimide, involving the amino-group of cysteine and resulting in scission of the succinimide ring, has been investigated. Evidence is presented that other maleimides react in a like manner.

N-Ethylmaleimide reacts rapidly with thiols forming a stable thio-ether link, and has had frequent application as a reagent for thiol groups of proteins.[1] However, as a marker of such groups it is of little value as it forms colourless derivatives. We report the preparation of a coloured maleimide, *N*-2,4-dinitroanilinomaleimide, which we have used to label protein thiols,[2] and we also describe a novel reaction with cysteine which appears to be general also for other maleimides.

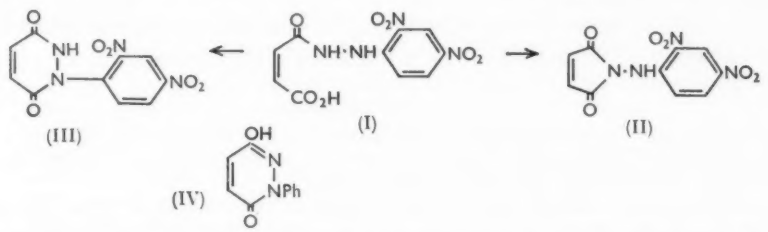
Compound	Solvent	Absorption bands in the region 1550—1800 cm.$^{-1}$
N-Ethylmaleimide [a]	$CHCl_3$	1712, 1594
N-(1-Naphthyl maleimide) [a]	$CHCl_3$	1745sh, 1724, 1602
N-2,4-Dinitroanilinomaleamic acid (I)	Nujol	1695, 1615sh, 1580
N-2,4-Dinitroanilinomaleimide (II)	CH_2Cl_2	1750, 1620, 1605sh
	Nujol	1730, 1620, 1595sh
p-Phenylazomaleanil	CH_2Cl_2	1715, 1595
1,6-Dihydro-3-hydroxy-6-oxo-1-phenylpyridazine (IV)	Nujol	1650, 1590, 1560
[IX; R = H, R′ = 2,4-$(NO_2)_2C_6H_3$·NH]	Nujol	1665, 1640sh, 1610, 1580
(IX; R = CO_2Me; R′ = *p*-Ph·N_2·C_6H_4·NH)	Nujol	1745, 1650, 1590
	CH_2Cl_2	1740, 1680, 1590

[a] Tsou, Barnett, and Seligman, *J. Amer. Chem. Soc.*, 1955, **77**, 4613.

Reaction of 2,4-dinitrophenylhydrazine with maleic anhydride gave the hydrazide (I) which was dehydrated in hot acetic acid. The latter step could result in the formation of either the maleimide (II) or the pyridazine derivative (III).

[1] Boyer, in "The Enzymes," (eds. Boyer, Lardy, and Myrback, Academic Press, New York, 1959), p. 511.
[2] Clark-Walker, unpublished work.

A decision in favour of the former was made on the basis of the infrared spectrum (see Table). The band at 1750 cm.$^{-1}$ in dichloromethane lies in the region associated with known maleimide-carbonyl frequencies. In contrast, the pyridazine derivative (IV)



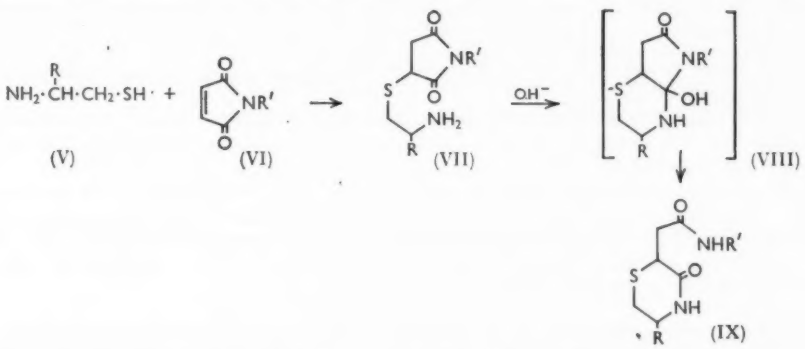
(III) (I) (II)

(IV)

which is obtained [3,4] by condensation of maleic anhydride and phenylhydrazine does not absorb above 1700 cm.$^{-1}$. We find that compound (IV), unlike maleimides and our product (II), gives a positive test with ferric chloride and is unreactive towards cysteine. It appears from these results that the effect of the nitro-groups on the benzene ring decreases the nucleophilic power of the α-nitrogen atom, causing condensation to occur at the β-nitrogen, whereas, in their absence the reaction occurs at the α-nitrogen.

Compound (II) was then tested for its reactivity towards cysteine and glutathione. These thiols added readily at room temperature and over the tested pH range of 3—8. However, chromatography with butanol–acetic acid–water indicated that at alkaline pH the cysteine addition compound (VII) [R = CO_2H, R′ = 2,4-$(NO_2)_2C_6H_3$·NH] rapidly gave a new substance with a greater R_F value and unreactive to ninhydrin. The glutathione addition compound showed no such change.

Attempts to isolate the resultant ninhydrin-negative compound proved unsuccessful as the product was always contaminated with the maleamic acid resulting from the hydrolysis of unchanged imide (II). By replacing cysteine with 2-mercaptoethylamine a similar masked amino-compound could be separated from all contaminants by ether-extraction under acid and alkaline conditions. A similar compound was prepared from



(V) (VI) (VII) (VIII) (IX)

p-phenylazomaleanil [5] and methyl-L-cysteine. The infrared spectra of the compounds are given in the Table. The carbonyl absorptions (1665, 1650, and 1680 cm.$^{-1}$) are substantially lower than those of the corresponding maleimides. The absorptions fall in the region associated with amide-carbonyl and indicate that the five-membered succinimide ring no longer exists. This evidence together with the affinity for non-polar solvents and

[3] Biquard and Grammaticakis, *Bull. Soc. chim. France*, 1942, **9**, 675.
[4] Druey, Huni, Meier, Ringier, and Staehelin, *Helv. Chim. Acta*, 1954, **37**, 510.
[5] Nayler and Whiting, *J.*, 1955, 297.

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ninhydrin-negativity indicates that the amino-group of the mercaptoethylamine, methylcysteine, and (by analogy) cysteine addition compounds has become involved in cyclization with the adjacent carbonyl group of the succinimide ring, leading to the formation of a substituted 1,4-thiazine (IX).

We have also observed the cyclization to occur with cysteine addition compounds of *N*-ethyl-, *N*-phenyl-, *N*-*p*-methoxyphenyl-,[6] and *N*-*p*-nitrophenyl-maleimide.[6]

Experimental

Chromatography.—Ascending paper chromatography was used with Whatman No. 1 paper with butanol–ethanol–ammonia (*d* 0·88)–water (200 : 47 : 3 : 88) and butanol–acetic acid–water (120 : 30 : 50). The solvents were renewed after 7 days.

Infrared Analyses.—Infrared spectra were obtained on a Perkin–Elmer recording spectrophotometer model 137 for Nujol mulls or 0·01M-solutions in dichloromethane.

Cyclization of Cysteine Product.—A solution of the maleimide (0·01 molar) in acetone was treated with an equal quantity of cysteine (0·01 molar) at room temperature for 10 min., then chromatographed in both the acid and the alkaline solvent for 5 hr. Cyclization was associated with disappearance of a free amino-group and was tested for by the use of a ninhydrin dipping reagent (0·3% in chloroform).

Preparations.—N-2,4-*Dinitroanilinomaleamic acid* (I). Maleic anhydride (16 g.) and 2,4-dinitrophenylhydrazine (30 g.) were refluxed in chloroform (350 ml.) with occasional shaking for ½ hr. After cooling, the orange solid was collected. Four crystallizations from acetone–benzene gave the *maleamic acid* as yellow needles, m. p. 194° (decomp.) (Found: C, 41·0; H, 3·1; N, 18·7. $C_{10}H_8N_4O_7$ requires C, 40·5; H, 2·7; N, 18·9%).

N-2,4-*Dinitroanilinomaleimide* (II). Compound (I) (5 g.) was refluxed in " AnalaR " acetic acid (50 ml.) for 10 min. The yellow *imide* crystallized (4 g.). Five crystallizations from acetone–benzene yielded pale yellow needles, m. p. 237° (decomp.) (Found: C, 43·3; H, 2·5; O, 34·1. $C_{10}H_6N_4O_6$ requires C, 43·2; H, 2·25; O, 34·5%), soluble in acetone but insoluble in benzene and water. In dilute alkali it gave a dark brown solution from which the amic acid could be recovered.

N^2-(2,4-*Dinitrophenyl*)-α-(*tetrahydro*-3-*oxo*-1,4-*thiazin*-2-*yl*)*acethydrazide* [IX; R = H, R′ = 2,4-$(NO_2)_2C_6H_3$·NH]. Compound (II) (1·5 g.) in acetone (20 ml.) was treated with an excess of 2-mercaptoethylamine hydrochloride (0·65 g.) in water (5 ml.). After 15 min. 0·1M-ammonium carbonate buffer (pH 9; 50 ml.) was added and the solution set aside. After 8 hr. ether was added; a precipitate was formed and was collected. Crystallization from acetone–water gave the *product* as yellow rods (0·8 g.) (Found: C, 41·0; H, 4·0; O, 27·4; S, 8·5. $C_{12}H_{13}N_5O_6S$ requires C, 40·6; H, 3·7; O, 27·0; S, 9·0%). The compound was unchanged when heated in toluene at 100° for 7 hr.

Methyl tetrahydro-5-*oxo*-6-(N^2-*phenylazophenylhydrazinocarbonylmethyl*)-1,4-*thiazine*-3-*carboxylate* (IX; R = CO_2Me, R′ = *p*-Ph·N_2·C_6H_4·NH). *p*-Phenylazomaleanil (0·2 g.) in acetone (10 ml.) was treated with an excess of methyl-L-cysteine (0·1 g.) in water (1 ml.). After 8 hr. at room temperature 5% aqueous ammonia and toluene were added until two phases formed. The toluene extract was washed with dilute mineral acid. Evaporation and crystallization of the residue from aqueous alcohol gave the *thiazine* as orange needles, m. p. 159—160°, $[\alpha]_D^{20}$ +16·8° (1% in $CHCl_3$) (Found: C, 58·3; H, 4·9; N, 13·3; S, 7·6. $C_{20}H_{20}N_4O_4S$ requires for C, 58·2; H, 4·9; N, 13·6; S, 7·8%).

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Department of Biochemistry, University of Western Australia,
Nedlands, Western Australia. [*Received, November 30th,* 1960.]

[6] Roderick, *J. Amer. Chem. Soc.*, 1957, **79**, 1710.

548. *The Rearrangement of 1-Hydroxyalkylphosphines to Alkylphosphine Oxides.*

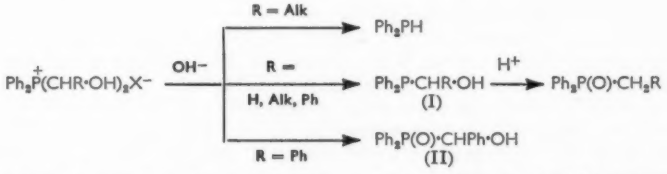
By S. Trippett.

Di-(1-hydroxyalkyl)diphenylphosphonium halides, treated with aqueous alkali to pH 9, give 1-hydroxyalkyldiphenylphosphines. The corresponding phosphine oxide and diphenylphosphine may also be formed. The 1-hydroxyalkylphosphines, with toluene-*p*-sulphonic acid, in refluxing acetic acid, rearrange to alkylphosphine oxides, but hydroxymethyldiphenylphosphine, with toluene-*p*-sulphonic acid, in refluxing toluene, gives diphenylphosphine. This reaction was applied to the conversion of phenylphosphine into methylphenylphosphine.

In an attempt to prepare bromomethyldiphenylphosphine, methoxymethyldiphenylphosphine (obtained by the reduction of the phosphine oxide with lithium aluminium hydride) was refluxed in acetic acid while dry oxygen-free hydrogen bromide was passed through the solution for 8 hr. The major product was methyldiphenylphosphine oxide. This was probably formed *via* the ion $Ph_2P{\cdot}\overset{+}{C}H_2 \longleftrightarrow Ph_2\overset{+}{P}{:}CH_2$; such ions would be formed from 1-hydroxyalkyldiphenylphosphines on suitable acid-treatment, and similar rearrangements were therefore sought among these compounds.

The 1-hydroxyalkyldiphenylphosphines, $Ph_2P{\cdot}CHR{\cdot}OH$ (R = H, Et, Pr^n, or Ph), all rearranged when refluxed in acetic acid with toluene-*p*-sulphonic acid, giving the alkylphosphine oxides, $Ph_2P(O){\cdot}CH_2R$. The hydroxymethylphosphine (I; R = H) also gave some 48% of the acetate, $Ph_2P{\cdot}CH_2{\cdot}OAc$, which was isolated as the methiodide. The high yield of acetate after a long reaction time indicates that it is not an intermediate in formation of the phosphine oxide.

The 1-hydroxyalkylphosphines were obtained by the action of aqueous alkali on di-(1-hydroxyalkyl)diphenylphosphonium halides, $[Ph_2P(CHR{\cdot}OH)_2]^+X^-$, themselves prepared from diphenylphosphine and an aldehyde under appropriate acidic conditions. Hydroxymethyl- and α-hydroxybenzyl-diphenylphosphine obtained in this way were free from diphenylphosphine, as shown by the absence of P–H absorption in the infrared spectrum at ~4·35 μ, but 1-hydroxyalkyl substituents proved to be very sensitive to alkali, and the crude 1-hydroxyalkylphosphines $Ph_2P{\cdot}CHR{\cdot}OH$ where R = Et or Pr^n contained about 70% of diphenylphosphine. The action of aqueous alkali on the di-(α-hydroxybenzyl)phosphonium salt also gave α-hydroxybenzyldiphenylphosphine oxide (II).



Buckler [1] has shown that the product from the reaction of phosphine, benzaldehyde, and hydrogen chloride in ether is benzyldi-(α-hydroxybenzyl)phosphine oxide, and suggested a secondary phosphine oxide, $Ph{\cdot}CH(OH){\cdot}PH(O){\cdot}CH_2Ph$, as an intermediate. Such an oxide could be formed by a rearrangement of di-(α-hydroxybenzyl)phosphine analogous to those described above; the observed product could also be formed by a similar rearrangement of tri-(α-hydroxybenzyl)phosphine.

When hydroxymethyldiphenylphosphine was refluxed in toluene with toluene-*p*-sulphonic acid, no phosphine oxide was formed. Instead paraformaldehyde accumulated

[1] Buckler, *J. Amer. Chem. Soc.*, 1960, **82**, 4215.

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in the condenser and diphenylphosphine (78%) was isolated. This ready removal of a hydroxymethyl group was used in the conversion of phenylphosphine into methylphenylphosphine. Phenylphosphine with formaldehyde and hydrochloric acid gave a solution containing tri(hydroxymethyl)phenylphosphonium chloride.[2] This solution, when made alkaline, gave di(hydroxymethyl)phenylphosphine, which on quaternisation with methyl iodide and treatment with alkali gave crude (hydroxymethyl)-methylphenylphosphine. Removal of the hydroxymethyl group gave methylphenylphosphine. The overall yield from phenylphosphine was low (15%). The secondary phosphine was characterised by reaction with benzyl bromide to give benzylmethylphenylphosphonium bromide. With aqueous alkali this gave benzylmethylphenylphosphine, identified as the methiodide. Similarly diphenylphosphine with benzyl bromide gave benzyldiphenylphosphonium bromide which with alkali gave the stable, crystalline, benzyldiphenylphosphine.

From the action of hydrogen bromide in acetic acid on methoxymethyldiphenylphosphine, the minor product, after treatment with methyl iodide, was dimethyldiphenylphosphonium iodide. Similarly the quaternary iodides obtained on rearrangement of the crude 1-hydroxyalkyldiphenylphosphines and treatment of the products with methyl iodide were mixtures of dimethyldiphenylphosphonium iodide and methyldiphenylphosphonium iodide. The dimethyldiphenylphosphonium iodide in each case probably arose from diphenylphosphine, although under ordinary conditions this with methyl iodide gives only methyldiphenylphosphonium iodide.

Experimental

Experiments involving phosphines were carried out under oxygen-free nitrogen. Unless otherwise stated, light petroleum refers to that fraction having b. p. 60—80°.

Methoxymethyldiphenylphosphine.—A suspension of methoxymethyltriphenylphosphonium chloride (50 g.) in N-sodium hydroxide (500 ml.) was refluxed for 0·5 hr., cooled, and extracted twice with benzene. The extract was dried and evaporated, and the residue crystallised from benzene–light petroleum to give *methoxymethyldiphenylphosphine oxide* (31 g.), m. p. 116—117° (Found: C, 68·2; H, 6·1. $C_{14}H_{15}O_2P$ requires C, 68·2; H, 6·1%).

The above phosphine oxide (24 g.) was added slowly to a stirred suspension of lithium aluminium hydride (8 g.) in di-n-butyl ether (200 ml.) on a boiling-water bath, the suspension was heated for 18 hr., then cooled in ice, and methanol (40 ml.) was added. Solvent was removed under reduced pressure and the residue distilled to give *methoxymethyldiphenylphosphine* (12 g.), b. p. 138—139°/0·1 mm. The *methiodide* had m. p. (from chloroform–ethyl acetate) 144—146° (Found: C, 48·45; H, 4·8. $C_{15}H_{18}IOP$ requires C, 48·4; H, 4·9%); the *benzylphosphonium bromide* had m. p. (from chloroform–ethyl acetate) 173—175° (Found: C, 63·1; H, 5·6. $C_{21}H_{22}BrOP$ requires C, 62·85; H, 5·5%).

Action of Hydrogen Bromide in Acetic Acid on Methoxymethyldiphenylphosphine.—A slow stream of oxygen-free hydrogen bromide was passed for 8 hr. through a refluxing solution of methoxymethyldiphenylphosphine (11 g.) in acetic acid (100 ml.). Solvent was then removed under reduced pressure, the residue taken up in benzene (100 ml.), methyl iodide (10 ml.) added, and the solution set aside at room temperature for 18 hr. Filtration gave dimethyldiphenylphosphonium iodide (3·2 g.), m. p. (from water) 250—251° (decomp.) (Found: C, 49·25; H, 4·8. Calc. for $C_{14}H_{16}IP$: C, 49·1; H, 4·7%). The mother-liquors, on evaporation and crystallisation of the residue from light petroleum (b. p. 80—100°), gave methyldiphenylphosphine oxide (7 g.), m. p. and mixed m. p. 112·5—113°.

Hydroxymethyldiphenylphosphine.—Diphenylphosphine (8 g.), 40% aqueous formaldehyde (15 ml.), concentrated hydrochloric acid (12 ml.), and water (40 ml.) were heated on a steam-bath for 1 hr., the clear solution cooled, and sodium iodide (15 g.) in water (10 ml.) added. The resulting syrup crystallised when rubbed with saturated aqueous sodium iodide and was filtered off and dried (13·5 g.).

The phosphonium iodide (10 g.) was dissolved in water (50 ml.), 2N-sodium hydroxide (20 ml.)

[2] Hellman and Schumacher, *Angew. Chem.*, 1960, **72**, 211.

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added, and the suspension extracted with chloroform (100 ml.). The extract was dried and evaporated to give hydroxymethyldiphenylphosphine (5·2 g.) [characterised as the *phosphine oxide*, m. p. (from benzene–light petroleum) 138—140°, $\lambda_{max.}$ 3·1, 8·65 μ (Found: C, 67·35; H, 5·75. $C_{13}H_{13}O_2P$ requires C, 67·2; H, 5·6%) and the *benzylphosphonium bromide*, m.p. (from chloroform–ethyl acetate) 220—222° (decomp.) (Found: C, 61·85; H, 5·2. $C_{20}H_{20}BrOP$ requries C, 62·0; H, 5·2%].

*Action of Toluene-*p*-sulphonic Acid in Acetic Acid on Hydroxymethyldiphenylphosphine.*—A solution of hydroxymethylphosphine (5·8 g.) and toluene-*p*-sulphonic acid (0·25 g.) in acetic acid (50 ml.) was refluxed for 6 hr., then evaporated under reduced pressure, and the residue in benzene (40 ml.) was treated with methyl iodide (5 ml.) for 3 hr. Filtration gave *acetoxymethyldiphenylphosphonium iodide* (4·25 g.), m. p. (from chloroform–ethyl acetate) 175—178°, $\lambda_{max.}$ 5·66 μ (Found: C, 47·9; H, 4·45. $C_{16}H_{18}IO_2P$ requires C, 48·0; H, 4·5%). The mother-liquors were evaporated and the residue, in chloroform, washed with sodium hydrogen carbonate solution and with water. The solution was dried and evaporated, and the residue crystallised from light petroleum (b. p. 80—100°) to give methyldiphenylphosphine oxide (2·8 g.), m. p. 111—112°.

*Action of Toluene-*p*-sulphonic Acid in Toluene on Hydroxymethyldiphenylphosphine.*—A solution of hydroxymethyldiphenylphosphine (13·5 g.) and toluene-*p*-sulphonic acid (0·25 g.) in toluene (100 ml.) was refluxed for 5·5 hr., and then distilled to give diphenylphosphine (9 g.), b. p. 150—152°/15 mm.

1-*Hydroxypropyldiphenylphosphine.*—Dry hydrogen chloride was passed through a solution of diphenylphosphine (5 g.) and propionaldehyde (5 ml.) in ether (75 ml.) at 0° until the first signs of stickiness in the resulting precipitate. Filtration then gave *di*-(1-*hydroxypropyl*)-*diphenylphosphonium chloride* (6 g.), m. p. (from ethyl acetate) 140° (decomp.) (Found: C, 64·0; H, 7·4. $C_{18}H_{24}ClO_2P$ requires C, 63·8; H, 7·1%).

The above phosphonium chloride (1·9 g.) in ethanol (20 ml.) was titrated with 2N-sodium hydroxide to pH 9, and the solution was diluted with water and extracted with chloroform. The extract was dried and evaporated. The infrared spectrum of the residue indicated that it was largely diphenylphosphine. It was taken up in acetic acid (15 ml.), toluene-*p*-sulphonic acid (0·25 g.) added, and the solution refluxed for 16 hr. Solvent was then removed under reduced pressure and the residue, in benzene (30 ml.), treated with methyl iodide (5 ml.) for 36 hr. The crude phosphonium iodide, m. p. 154—158°, was then filtered off and the filtrate washed with aqueous sodium carbonate and with water, dried, and evaporated. Crystallisation of the residue from ethyl acetate–light petroleum gave *diphenylpropylphosphine oxide* (0·45 g.), m. p. and mixed m. p. 100—101°. An authentic sample, m. p. 100—101° (Found: C, 73·6; H, 7·0. $C_{15}H_{17}OP$ requires C, 73·7; H, 7·0%), was prepared by the alkaline hydrolysis of triphenylpropylphosphonium iodide.

1-*Hydroxybutyldiphenylphosphine.*—Dry hydrogen chloride was passed through a solution of diphenylphosphine (5 g.) and butyraldehyde (7 ml.) in ether (75 ml.) at 0°, and the resulting precipitate filtered off. Crystallisation from ethyl acetate gave *di*-(1-*hydroxybutyl*)*diphenylphosphonium chloride* (8·3 g.), m. p. 127° (decomp.) (Found: C, 65·3; H, 7·6. $C_{20}H_{28}ClO_2P$ requires C, 65·4; H, 7·7%).

A solution of the above phosphonium chloride (8 g.) in water (100 ml.) was made alkaline to phenolphthalein with 2N-sodium hydroxide and extracted thrice with chloroform, and the combined extracts were dried and evaporated. The residue (4·8 g.), largely diphenylphosphine, was dissolved in acetic acid (50 ml.) with toluene-*p*-sulphonic acid (0·3 g.), and the solution was refluxed for 5 hr. Solvent was then removed under reduced pressure and the residue, in benzene (30 ml.), treated with methyl iodide (5 ml.) at room temperature overnight. The mixed phosphonium iodides, m. p. 154—158°, were filtered off and the filtrate washed twice with water, dried, and evaporated. After passage, in benzene, through a small column of alumina, the residue crystallised from ethyl acetate–light petroleum (b. p. 80—100°) to give *butyldiphenylphosphine oxide* (1·1 g.), m. p. 93—94°. An authentic sample, m. p. 93—94° (Found: C, 74·5; H, 7·35. $C_{16}H_{19}OP$ requires C, 74·3; H, 7·4%), was prepared by the alkaline hydrolysis of butyltriphenylphosphonium bromide.

The mixed phosphonium iodides, m. p. 154—158°, $\lambda_{max.}$ 4·1—4·2 μ, on crystallisation from chloroform–ethyl acetate and then from water, gave dimethyldiphenylphosphonium iodide, m. p. and mixed m. p. 250—251°. When dissolved in warm water, and the cooled solution extracted with ether, they gave methyldiphenylphosphine, identified as the allylphosphonium

bromide, m. p. 167—169° (lit.,[3] m. p. 161°) (Found: C, 59·55; H, 5·7. Calc. for $C_{16}H_{18}IP$: C, 59·7; H, 5·4%).

Diphenylphosphine and methyl iodide in benzene at room temperature overnight gave *methyldiphenylphosphonium iodide*, m. p. 162—163° (Found: C, 47·7; H, 4·3. $C_{13}H_{14}IP$ requires C, 47·6; H, 4·3%).

α-Hydroxybenzyldiphenylphosphine.—Dry hydrogen chloride was passed into a solution of diphenylphosphine (5 g.) and benzaldehyde (5 g.) in ether (150 ml.), and the resulting precipitate was filtered off and crystallised from ethyl acetate–ether to give *di-(α-hydroxybenzyl)diphenylphosphonium chloride* (8·1 g.), m. p. 165—170° (Found: C, 72·3; H, 5·3. $C_{26}H_{24}ClO_2P$ requires C, 71·8; H, 5·5%).

A suspension of this phosphonium chloride (10 g.) in water (150 ml.) and chloroform (100 ml.) was shaken while 2N-sodium hydroxide was added slowly till the aqueous layer was alkaline to phenolphthalein. The chloroform was then dried and evaporated, and the residue taken up in benzene (40 ml.) and allowed to crystallise. Filtration gave α-hydroxybenzyldiphenylphosphine oxide, m. p. (from aqueous ethanol) 177—179° (lit.,[4] m. p. 178—179·5°) (Found: C, 74·1; H, 5·75. Calc. for $C_{19}H_{17}O_2P$: C, 74·0; H, 5·5%). The filtrate was evaporated and the residue, which showed no P–H absorption in the infrared spectrum, was taken up in acetic acid (40 ml.), toluene-*p*-sulphonic acid (0·25 g.) added, and the solution refluxed for 8 hr. Solvent was then removed under reduced pressure and the residue crystallised from benzene, to give benzyldiphenylphosphine oxide (2·6 g.), m. p. 195—196° (lit.,[5] m. p. 196°) (Found: C, 78·3; H, 5·9. Calc. for $C_{19}H_{17}OP$: C, 78·0; H, 5·8%).

Benzyldiphenylphosphonium Bromide.—A solution of diphenylphosphine (2 g.) and benzyl bromide (5 g.) in benzene (20 ml.) was set aside at room temperature for 5 days. The resulting sticky solid was rubbed with ethyl acetate and then crystallised from chloroform–ethyl acetate, to give *benzyldiphenylphosphonium bromide* (2·1 g.), m. p. 202—204° (Found: C, 64·3; H, 5·1. $C_{19}H_{18}BrP$ requires C, 63·8; H, 5·1%). The hydrobromide was warmed on a steam-bath with 2N-sodium hydroxide for a few minutes, and the resulting solid crystallised from aqueous ethanol to give *benzyldiphenylphosphine*, m. p. 74° (Found: C, 82·7; H, 6·4. $C_{19}H_{17}P$ requires C, 82·5; H, 6·2%). The *methiodide* had m. p. (from ethanol) 243—245° (Found: C, 57·3; H, 4·6. $C_{20}H_{20}IP$ requires C, 57·5; H, 4·8%).

Methylphenylphosphine from Phenylphosphine.—Phenylphosphine (15 g.), 40% aqueous formaldehyde (36 ml.), concentrated hydrochloric acid (30 ml.), and water (100 ml.) were heated on a steam-bath for 1 hr., and the resulting solution was cooled in ice, made alkaline to phenolphthalein with 10N-sodium hydroxide, and extracted thrice with chloroform. The extracts were dried and evaporated, the residue (19·5 g.) was dissolved in benzene (100 ml.) at 0°, methyl iodide (8 ml.) added, and the solution set aside at room temperature overnight. Solvent was then removed, the residue dissolved in water (200 ml.), and the solution made alkaline to phenolphthalein with 2N-sodium hydroxide and extracted with chloroform. The extracts were dried and evaporated, and the residue (11·5 g.), with toluene-*p*-sulphonic acid (0·3 g.), was refluxed in toluene (50 ml.) for 8 hr. Distillation then gave methylphenylphosphine (2·6 g.), b. p. 60—62°/13 mm., $\lambda_{max.}$ 4·3 μ(s). With benzyl bromide in benzene at room temperature for 4 days, this gave *benzylmethylphenylphosphonium bromide*, m. p. (from chloroform–ethyl acetate) 159—160°, $\lambda_{max.}$ 4·1—4·3 μ (Found: C, 56·85; H, 5·65. $C_{14}H_{16}BrP$ requires C, 56·95; H, 5·5%). The hydrobromide was shaken with 2N-sodium hydroxide and chloroform, the chloroform dried and evaporated, and the residue treated with methyl iodide in benzene to give *benzyldimethylphenylphosphonium iodide*, m. p. (from chloroform–ethyl acetate) 168—169° (Found: C, 50·3; H, 5·1. $C_{15}H_{18}IP$ requires C, 50·55; H, 5·1%).

THE UNIVERSITY, LEEDS, 2. [*Received, January 16th*, 1961.]

[3] Meisenheimer and Lichtenstadt, *Annalen*, 1926, **449**, 213.
[4] Miller, Miller, Rogers, and Hamilton, *J. Amer. Chem. Soc.*, 1957, **79**, 424.
[5] Michaelis and LaCoste, *Ber.*, 1885, **18**, 2109.

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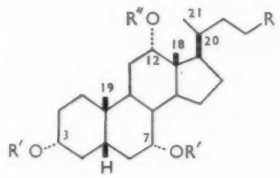
549. *Scymnol Sulphate and Anhydroscymnol.*

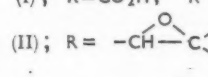
By A. D. Cross.

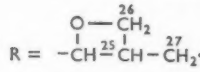
Anhydroscymnol, the product of alkaline hydrolysis of scymnol sulphate,[1] has been shown to contain a trimethylene oxide ring (IIIa). The nomenclature, structures, and biogenesis of some bile alcohol sulphates and the derived alcohols are commented upon.

Hammarsten [2] isolated α-scymnolsulphuric acid from the bile of the shark *Scymnus borealis*. The homogeneity of his "β-scymnolsulphuric acid" remains unsubstantiated. Isolation of the α-form, more commonly termed scymnol sulphate, from rays and other sharks has been reported,[3] and Cook [3] considered it a typical component of the bile of Elasmobranch fishes. Vigorous alkali hydrolysis furnished a free bile alcohol, scymnol.[2-7] In view of the structure established here for this compound, and from the known properties of other bile alcohol sulphate esters, it is proposed that this hydrolysis product be renamed anhydroscymnol, which name is employed throughout this communication.*



(I); R = CO_2H; R′ = R″ = H

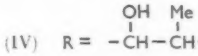
(II); R =  ; R′ = R″ = H

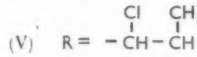
(III); R = 

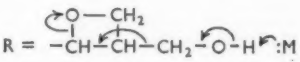
(a); R′ = R″ = H

(b); R′ = Ac; R″ = H

(c); R′ = R″ = Ac

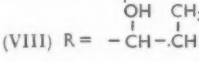
(IV) R =  ; R′ = R″ = H

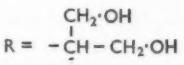
(V) R =  ; R′ = R″ = H

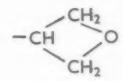
(VI) R = 

R′ = R″ = H

(VII) R = ; R′ = R″ = H

(VIII) R =  ; R′ = R″ = H

(IX) R = 

(X) R = 

Early work established the presence in anhydroscymnol of one primary and three secondary hydroxyl groups, and an oxide ring opened by hydrogen chloride to a chlorohydrin from which the oxide ring was regenerated by the action of alkali.[5] Oxidation of anhydroscymnol tetra-acetate, followed by hydrolysis, gave cholic acid (I).[6,7] Structure

* The proposed change standardises the nomenclature for hydrolysis products of bile alcohol sulphates.

[1] In a preliminary account of this work (Cross, *Proc. Chem. Soc.*, 1960, 344), the expression "scymnol," the hydrolysis product of a constituent of shark bile was incorrectly abbreviated.

[2] Hammarsten, *Z. physiol. Chem.*, 1898, **24**, 322.

[3] Cook, *Nature*, 1941, **147**, 388; Igarashi and Kakubata, *Mem. Fac. Agric., Hokkaido Univ.*, 1952, **1**, 181; Oikawa, *J. Biochem.* (*Japan*), 1925, **5**, 63.

[4] Fieser and Fieser, "Natural Products Related to Phenanthrene," 3rd Edn., Reinhold Publ. Corp., New York, 1949, pp. 112—113.

[5] Windaus, Bergmann, and König, *Z. physiol. Chem.*, 1930, **189**, 148.

[6] Asikari, *J. Biochem.* (*Japan*), 1939, **29**, 319.

[7] Bergmann and Pace, *J. Amer. Chem. Soc.*, 1943, **65**, 477.

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(II) for anhydroscymnol [6] was accepted until Fieser and Fieser [4] remarked on the improbability of the epoxide (II) remaining inert during the vigorous oxidation of anhydroscymnol to a trioxo-carboxylic acid.[5] A trimethylene oxide structure (IIIa) appeared more acceptable and the applicability of nuclear magnetic resonance spectroscopy to the structural problem was noted.[8]

Acetylation of anhydroscymnol afforded the triacetate (IIIb) [showing infrared absorption at 3632 $cm.^{-1}$ (OH)] and the tetra-acetate (IIIc).* Assignment of the unacetylated hydroxyl group to the 12α-position (IIIb) follows from molecular-rotation changes coincident upon further acetylation,[1] and from the known hindrance to attack at this position by the side-chain. In the nuclear magnetic resonance spectrum neither anhydroscymnol triacetate (in chloroform) nor scymnol sulphate (in pyridine) showed absorption assignable to epoxide protons or to a methyl group attached to a carbon atom also bearing oxygen,[9] except acetates, thus rendering untenable structure (II) for anhydroscymnol. Reduction of anhydroscymnol with lithium aluminium hydride furnished dihydroanhydroscymnol (deoxyscymnol) (IV). Slomp and Mackellar [10] recently recorded nuclear magnetic resonance spectra of hydroxylated steroids in pyridine solutions and observed that, compared with spectra of solutions in halogenated hydrocarbons, the *C*-methyl proton absorp-

Nuclear magnetic resonance: methyl-proton absorption data.[a]

Protons (no.)	18-Methyl (3)	19-Methyl (3)	21-Methyl [d] (3)	26-Methyl [d] (3)	Acetyl (various)
Methyl cholate in C_5H_5N	9·20 (2·6)	9·00 (3·1)	8·84, 8·78 (3·3)	—	—
Methyl 3α,12α-diacetyl-7-deoxycholate in $CHCl_3$	9·28	9·09	9·17 [g]	—	7·97, 7·90
Methyl 3α,7α,12α-triacetylcholate in CCl_4	9·27	9·08	9·16, 9·11	—	8·05, 7·96, 7·93
Anhydroscymnol in C_5H_5N	9·20 (2·6)	9·00 (2·8)	8·83, 8·76 (3·6)	—	—
Anhydroscymnol triacetate { in $CHCl_3$	9·31	9·07	8·98 [g]	—	7·96 (3), 7·92 (6)
Anhydroscymnol triacetate { in C_5H_5N	9·28	9·11	8·86, 8·81	—	8·14 (3), 8·00 (6)
Anhydroscymnol tetra-acetate in CCl_4	9·27	9·07	9·17, 9·12	—	8·03, 7·99, 7·94, 7·91
Dihydroanhydroscymnol in C_5H_5N	9·18 (2·7)	9·00 (2·7)	8·83, 8·77, 8·71 (total 6·6)		—
Anhydroscymnol chlorohydrin in C_5H_5N	9·19	8·98	8·79, 8·74	—	—

[a] Absorptions are expressed as τ [b] values. Spectra were obtained with a Varian Associates V-4300 spectrometer equipped with a 56·445 megacycle oscillator and using *ca.* 10% solutions in chloroform, carbon tetrachloride, or pyridine.[c] Tetramethylsilane was used as an internal reference for calibration by the conventional sideband technique. [b] Tiers, *J. Phys. Chem.*, 1958, **62**, 1151. [c] Pyridine was purified by gas-liquid chromatography. [d] Secondary *C*-methyl absorption was never well-resolved [e] and consisted of a main peak with a shoulder at a higher τ value (splitting 3—4 c.p.s.). [e] A simple well-resolved doublet is not expected for a methyl group in the situation CHMe if the chemical shift between the two types of proton is of the same order as the coupling constant between them.[f] [f] Abraham, Pople, and Bernstein, *Canad. J. Chem.*, 1958, **36**, 1302. [g] The marked shift of this proton absorption on complete acetylation illustrates the steric proximity of the $C_{(21)}$-methyl to the 12α-hydroxyl.

tions are often shifted, with clarification of the spectrum. Our spectral results (see Table) confirm their observations and, moreover, establish that reduction of the oxide ring of

* "Scymnol" (anhydroscymnol) and some derivatives from the late Professor Bergmann's collection were made available through the kindness of Dr. W. M. Stokes, Providence College, Rhode Island, U.S.A.

[8] Cross, *Quart. Rev.*, 1960, in the press. L. F. Fieser, *Nucleus*, 1959, Dec., p. 80 (the Author thanks the Editor for drawing attention to this published lecture).

[9] For characteristic absorptions of methyl protons in various environments see Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, Ch. 4.

[10] Slomp and MacKellar, *J. Amer. Chem. Soc.*, 1960, **82**, 999.

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anhydroscymnol generates a new methyl group attached to a carbon atom bearing one hydrogen but no oxygen atom. Approximate area counts support this conclusion (see Table). Methyl cholate shows the same *C*-methyl proton absorption τ values and areas as anhydroscymnol and the derived chlorohydrin (V), all in pyridine solution: similarly, for carbon tetrachloride solution, *C*-methyl proton absorption of methyl triacetylcholate strongly resembles that of anhydroscymnol tetra-acetate.

In the infrared spectrum (potassium chloride disc) anhydroscymnol shows absorptions at 961 (s) and 878 cm.$^{-1}$ (w) attributed to the trimethylene oxide [11] since in the chlorohydrin (V), dihydroanhydroscymnol (IV), and scymnol sulphate, both bands are absent, removal of the former revealing the weak absorption (*ca.* 950 cm.$^{-1}$) of the cholic acid nucleus.

Support for structure (IIIa) for anhydroscymnol came from the failure of periodic acid to attack either dihydroanhydroscymnol or anhydroscymnol chlorohydrin. In each case structure (II) for anhydroscymnol requires oxidisable molecules. An early sample † labelled " periodic acid oxidation product of scymnol chlorohydrin " showed no carbonyl absorption in the infrared spectrum and, on recrystallisation, proved to be anhydroscymnol chlorohydrin hydrate. When heated with copper–bronze both anhydroscymnol and dihydroanhydroscymnol yielded formaldehyde. This reaction is characteristic of the 1,3-glycol system $>CH(OH)\cdot C\cdot CH_2\cdot OH$,[12] but with anhydroscymnol constitutes a new example of " fragmentation " [13] in which relief of the oxide ring strain promotes the reaction (VI ⟶ VII + H·CHO).[3] Barton and Brooks,[14] and Tarbell and his co-workers,[15] have described formally analogous C–C bond cleavages in αβ-epoxy-δ-hydroxy-systems of morolic acid and fumagillin derivatives, respectively, with aluminium hydride as the proton acceptor.

These observations are compatible solely with structures for anhydroscymnol (IIIa), scymnol (revised nomenclature) (VIII), and scymnol sulphate (VIII, sulphated on a side-chain hydroxyl group *). Scymnol, the hexol, still awaits preparation, and anhydroscymnol is an artefact of the hydrolytic method, a possibility envisaged by Haslewood a decade ago,[16] and now independently proved.[17] Reassessment of Hammarsten's analytical figures [2] for sodium scymnol sulphate revealed their better agreement with structure (VIII, monosulphated), $C_{27}H_{47}O_5\cdot SO_4Na$, than his suggested formula $C_{27}H_{45}O_4\cdot SO_4Na$.

Sodium ranol sulphate is found in the bile of the frog *Rana temporia*.[18] Acidic and alkaline hydrolyses lead respectively to ranol and anhydroranol, and evidence for a trimethylene oxide ring in the latter is being sought. Scymnol sulphate represents an interesting departure from the hitherto-assumed β-oxidative degradation of the cholesterol side-chain since both terminal methyl groups are now oxidised. It is considered very probable that other C_{27} bile alcohols incorporate this structural unit (IX), and the recent isolation of the first disulphate bile ester from the hagfish [19] is in accord with this notion. These C_{27} bile alcohols are found only in fishes and amphibia, and the side-chain structure of the bile alcohol sulphate of the coelacanth [20] is of obvious interest. Extension of this work will cover other bile alcohols and a search for the terminal structural unit (X).

* Though attachment of the sulphate ester at the $C_{(26)}$ or $C_{(27)}$ primary hydroxyl group is probable, published evidence does not yet exclude esterification at the $C_{(24)}$ hydroxyl group, which would give a mechanistically more favourable structural unit for formation of the trimethylene oxide ring (III).

[11] Barrow and Searles, *J. Amer. Chem. Soc.*, 1953, **75**, 1175, quote strong absorption at 970—980 cm.$^{-1}$ for simple trimethylene oxides. Gates and Roe, *Tetrahedron*, 1960, **11**, 148, have summarised data for similar absorptions, and all bands appear in the range 940—985 cm.$^{-1}$.
[12] Tsuda and Kitigawa, *Ber.*, 1938, **71**, 1604.
[13] Grob, *Experientia*, 1957, **13**, 126.
[14] Barton and Brooks, *J.*, 1951, 257.
[15] Tarbell, Carman, Chapman, Huffman, and McCorkindale, *J. Amer. Chem. Soc.*, 1960, **82**, 1005.
[16] Haslewood, *Biochem. Soc. Symp.*, 1951, **6**, 83.
[17] Briggs and Haslewood, *Biochem. J.*, in the press.
[18] Haslewood, *Biochem. J.*, 1952, **51**, 139.
[19] Haslewood, *Biochem. J.*, in the press.
[20] Haslewood, *Biochem. J.*, 1957, **66**, 22.

Experimental

Melting points were taken on a Kofler block. Analyses were determined by Miss Cuckney and her staff, infrared spectra by Mrs. Boston on a Grubb Parsons S4/DB1 spectrophotometer with calcium fluoride and sodium chloride prisms as appropriate, and nuclear magnetic resonance spectra by Dr. J. W. Lown. Light petroleum refers to the fraction, b. p. 60—80°.

Acetylation of Anhydroscymnol.—Anhydroscymnol (50 mg.) was treated with acetic anhydride (0·5 ml.) and pyridine (3 ml.) at room temperature during 24 hr. ***Anhydroscymnol triacetate*** (51 mg.) crystallised from chloroform–light petroleum as needles, m. p. 169—171°, $[\alpha]_D$ 34·4° (*c* 1·03 in $CHCl_3$) and 44·2° (*c* 1·96 in pyridine); infrared absorption peaks were at 3632 (OH) and 1734 cm.$^{-1}$ with shoulders at 1748 and 1743 cm.$^{-1}$ (3 acetates) (Found: C, 68·5; H, 9·2; Ac, 21·9. $C_{33}H_{52}O_8$ requires C, 68·7; H, 9·1; 3 Ac, 22·4%).

Chromatography on Grade III alumina of " acetylated scymnol," * prepared by keeping anhydroscymnol in pyridine with acetic anhydride at 100° during 1 hr., furnished anhydroscymnol triacetate and anhydroscymnol tetra-acetate. The latter crystallised from light petroleum as needles, m. p. 147—150° (lit.[7] 145—147°), $[\alpha]_D$ 75·8° (*c* 1·51 in $CHCl_3$) and 84·9° (*c* 1·70 in pyridine); no infrared hydroxyl absorption.

Dihydroanhydroscymnol.—Anhydroscymnol (100 mg.) in dry dioxan (10 ml.) was added to an excess of lithium aluminium hydride (100 mg.) in boiling dioxan (10 ml.), and the mixture kept boiling for 3 days. The excess of hydride was destroyed (ethyl acetate) and, after dilution (H_2O) of the mixture, dioxan was removed by azeotropic distillation. Saturated sodium potassium tartrate solution was then added and the suspension extracted continuously with hot chloroform for 2 days to yield *dihydroanhydroscymnol* (93 mg.), which crystallised as the monohydrate from ethanol–light petroleum or " wet " ethyl acetate as prisms, m. p. 118—124°, and 182—183° after resolidification or after being dried for 48 hr. at 105°. The m. p. of a mixture with anhydroscymnol (m. p. 189—190°) was 165—173°. Anhydroscymnol had $[\alpha]_D$ 39·1° (*c* 0·93 in pyridine) and dihydroanhydroscymnol $[\alpha]_D$ 36·2° (*c* 0·72 in pyridine) (Found, in sample dried at 105°: C, 68·8; H, 10·7. $C_{27}H_{48}O_5,H_2O$ requires C, 68·9; H, 10·7%). The solvent of crystallisation was removed during 48 hr. at 125° (Found: C, 71·4; H, 10·9. $C_{27}H_{48}O_5$ requires C, 71·6; H, 10·7%).

In an alternative procedure, after destruction of the excess of hydride, the hot aqueous dioxan solution was filtered and evaporated and dihydroanhydroscymnol extracted from the residue in 94% yield by 1 : 1 acetone–chloroform.

Glycol Reactions.—(a) *Periodic acid.* Dihydroanhydroscymnol in methanol was treated with aqueous periodic acid (0·02N; 10 ml.). A blank was similarly prepared but the sterol was omitted, and consumption of periodic acid was followed by iodometric titration. No periodic acid was consumed after 24 hr. at room temperature. The product was a gum showing strong hydroxyl but no carbonyl absorption in the infrared spectrum.

Anhydrous anhydroscymnol chlorohydrin, m. p. 196°, after treatment with periodate,* gave as the sole isolable compound anhydroscymnol chlorohydrin monohydrate, m. p. 132—135° (lit.,[5] m. p. 126°; Kofler block m. p. 130—135° for an authentic sample), showing no carbonyl absorption in the infrared spectrum.

(b) *Pyrolyses with copper–bronze.* An intimate mixture of powdered dihydroanhydroscymnol (80 mg.) and copper–bronze powder (200 mg.) was heated to 270—300° (metal bath) for 2 hr. in a stream of oxygen-free, dry nitrogen. Effluent gases were bubbled through freshly-prepared, ice-cold, aqueous dimedone solution. The precipitate was filtered off and, after recrystallisation from ethanol, identified as formaldehyde dimethone by m. p., mixed m. p., and comparative infrared spectra. A " blank " reaction, run simultaneously, gave no formaldehyde.

Anhydroscymnol similarly afforded formaldehyde dimethone under identical reaction conditions.

Acetylation of Dihydroanhydroscymnol.—Dihydroanhydroscymnol (55 mg.) was acetylated at room temperature as described for anhydroscymnol. Chromatography of the crude product on Grade III alumina yielded only a gum (30 mg.), chromatographically homogeneous, which appeared, from analysis, to be *dihydroanhydroscymnol tetra-acetate*, showing infrared absorption at 3545 cm.$^{-1}$ (hydroxyl) (Found: Ac, 26·3. $C_{35}H_{56}O_9$ requires 4 Ac, 27·7%). The nuclear

* See footnote on p. 2818.

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magnetic resonance spectrum showed proton absorption equivalent to two secondary *C*-methyl groups (cf. dihydroanhydroscymnol, Table).

The author is indebted to Professor D. H. R. Barton for his encouragement, and to Professor G. A. D. Haslewood for a sample of scymnol sulphate, for notification of unpublished results, and for stimulating discussion.

Department of Chemistry, Imperial College, South Kensington, London, S.W.7.
[Present address: Research Laboratories, Syntex S.A., Apartado 2679, Mexico, D.F.] [*Received, January 27th*, 1961.]

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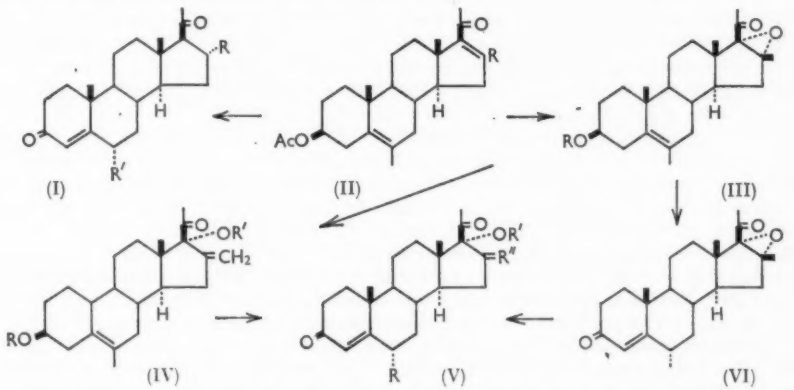
550. *Modified Steroid Hormones. Part XXII.*[1] 6α,16α-*Dimethylprogesterone and* 17α-*Acetoxy*-6α-*methyl*-16-*methyleneprogesterone.*

By D. N. Kirk, V. Petrow, and D. M. Williamson.

The preparation of the two compounds named in the title, from 3β-acetoxy-6-methylpregna-5,16-dien-20-one (II; R = H), is described.

6-Methylation of progesterone (I; R = R′ = H) and 17α-acetoxyprogesterone (V; R = H, R′ = Ac, R″ = H_2) leads to enhancement of progestational activity. The introduction of a 16-methylene group into the last compound is likewise accompanied by increase in biological potency. The preparation of the 6,16-disubstituted derivatives of progesterone and 17α-acetoxyprogesterone was consequently deemed to be of interest.

6α,16α-Dimethylprogesterone (I; R = R′ = Me) was obtained by using the readily available 3β-acetoxy-6-methylpregna-5,16-dien-20-one (II; R = H) as starting material. Reaction of this acetoxy-ketone with methylmagnesium iodide gave 3β-hydroxy-6,16α-dimethylpregn-5-en-20-one, mixed with 6-methylbisnorchola-5,16-diene-3,20-diol, from which it was separated by means of its ether-insoluble semicarbazone. Oppenauer oxidation then furnished the diketone (I; R = R′ = Me).



3β-Acetoxy-6-methylpregna-5,16-dien-20-one (II; R = H) condensed with diazomethane, to give 3β-acetoxy-6-methylpyrazolino(3′,4′-17α,16α)pregn-5-en-20-one. Pyrolysis of the last compound furnished 3β-acetoxy-6,16-dimethylpregna-5,16-dien-20-one (II; R = Me), which was oxidised by alkaline hydrogen peroxide to 16α,17α-epoxy-3β-hydroxy-6,16β-dimethylpregn-5-en-20-one (III; R = H). Oppenauer oxidation gave 16α,17α-epoxy-6α,16β-dimethylpregn-4-ene-3,20-dione (VI).

[1] Part XXI, *J.*, 1961, 2091.

Earlier work [2] in this laboratory had established the conversion of 16α,17α-epoxy-16β-methylpregnan-20-ones into 17α-hydroxy-16-methylenepregnan-20-ones under the influence of hydrogen ions. In accordance therewith, reaction of our product (VI) with a catalytic quantity of sulphuric acid in dioxan furnished 17α-hydroxy-6α-methyl-16-methylenepregn-4-ene-3,20-dione (V; R = Me, R′ = H, R″ = CH_2). Forced acetylation gave 3,17α-diacetoxy-6-methyl-16-methylenepregna-3,5-dien-20-one, which was converted into the required 17α-acetoxy-6α-methyl-16-methylenepregn-4-en-3-one (V; R = Me, R′ = Ac, R″ = CH_2) by cautious alkaline hydrolysis.

In examining an alternative route to the last compound, the 3-hydroxy-derivative (III; R = H) was acetylated and the product treated with an excess of hydrogen bromide in acetic acid. The product, however, proved to be 3β-acetoxy-6,16-dimethylpregna-5,14,16-trien-20-one in place of the required 3β-acetoxy-17α-hydroxy-6-methyl-16-methylenepregn-5-en-20-one (IV; R = Ac, R′ = H). The latter was obtained, however, by treating the acetylated epoxide (III; R = Ac) with a molar equivalent of a 50% w/v solution of hydrogen bromide in acetic acid–dioxan or with a catalytic quantity of sulphuric acid in tetrahydrofuran. Forced acetylation of the 17α-hydroxy-derivative (IV; R = Ac, R′ = H) with acetic anhydride and toluene-*p*-sulphonic acid in acetic acid gave a *ca.* 1 : 1 mixture of 3β,17α-diacetoxy-6-methyl-16-methylenepregn-5-en-20-one (IV; R = R′ = Ac) and 3β-acetoxy-6,16-dimethylpregna-5,14,16-trien-20-one. By omitting acetic acid from the acetylation mixture, however, the pure diacetate (IV; R = R′ = Ac) could be obtained in excellent yield. Its partial hydrolysis with methanolic hydrochloric acid furnished the 3-hydroxy-derivative (IV; R = H, R′ = Ac), which was converted into the required ketone (V; R = Me, R′ = Ac, R″ = CH_2) by Oppenauer oxidation.

Experimental

Rotations were determined in a 1 dm. tube for $CHCl_3$ solutions unless otherwise stated. Ultraviolet absorption spectra (of EtOH solutions) were kindly determined by Mr. M. T. Davies, B.Sc. Alumina (B.D.H. chromatography grade) was used throughout.

3β-*Acetoxy*-6-*methylpyrazolino*(3′,4′-17α,16α)*pregn*-5-*en*-20-*one*.—3β-Acetoxy-6-methylpregna-5,16-dien-20-one (20 g.) was treated with an ethereal solution of diazomethane prepared from *N*-methyl-*N*-nitrosotoluene-*p*-sulphonamide (30 g.). After 18 hr. at room temperature, the ether and excess of diazomethane were distilled off and the residue crystallised from methanol, to give the *pyrazoline* as plates, m. p. 156—158° (decomp.), $[\alpha]_D^{24}$ +7° (*c* 0·44) (Found: C, 72·6; H, 8·8; N, 6·9. $C_{25}H_{36}N_2O_3$ requires C, 72·7; H, 8·8; N, 6·8%).

3β-*Acetoxy*-6,16-*dimethylpregna*-5,16-*dien*-20-*one* (II; R = Me).—The foregoing pyrazoline (20 g.) was heated in dibutyl ether (200 ml.) under reflux for 3 hr. The butyl ether was removed under reduced pressure and the residue crystallised from methanol, to give 3β-*acetoxy*-6,16-*dimethylpregna*-5,16-*dien*-20-*one*, plates, m. p. 158—160°, $[\alpha]_D^{23}$ −99° (*c* 0·65), $\lambda_{max.}$ 251 mμ (log ε 3·94) (Found: C, 77·8; H, 9·4. $C_{25}H_{36}O_3$ requires C, 78·1; H, 9·4%).

3β-*Hydroxy*-6,16β-*dimethyl*-16α,17α-*epoxypregn*-5-*en*-20-*one* (III; R = H).—To a solution of the foregoing diene (5 g.) in boiling ethanol (50 ml.) containing 40% aqueous sodium hydroxide (2·5 ml.), 30% hydrogen peroxide (10 ml.) was added dropwise. Heating was continued for a further 30 min. The crystalline product was collected and purified from methanol, to give 3β-*hydroxy*-6,16β-*dimethyl*-16α,17α-*epoxypregn*-5-*en*-20-*one* (III; R = H), m. p. 161—162°, $[\alpha]_D^{23}$ −17° (*c* 0·94) (Found: C, 75·4; H, 10·0. $C_{23}H_{34}O_3,\frac{1}{2}H_2O$ requires C, 75·2; H, 9·6%).

3β-*Acetoxy*-16α,17α-*epoxy*-6,16β-*dimethylpregn*-5-*en*-20-*one* (III; R = Ac), needles (from methanol), m. p. 118—120°, $[\alpha]_D$ −49° (*c* 0·35), was prepared by acetylation with acetic anhydride–pyridine at 100° for 1 hr. (Found: C, 75·1; H, 9·0. $C_{25}H_{36}O_4$ requires C, 75·0; H, 9·0%).

16α,17α-*Epoxy*-6α,16β-*dimethylpregn*-4-*ene*-3,20-*dione* (VI).—16α,17α-Epoxy-3β-hydroxy-6,16β-dimethylpregn-5-en-20-one (5 g.) was dissolved in cyclohexanone (60 ml.) and the solution distilled until 10 ml. of distillate had been collected. Aluminium t-butoxide (5 g.) in dry toluene (40 ml.) was added and the mixture was heated under reflux for 45 min. Rochelle salt

[2] Kirk, Petrow, Stansfield, and Williamson, *J.*, 1960, 2385.

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solution was added and the mixture was steam-distilled for 6 hr. The product was isolated with chloroform and crystallised from methanol. **16α,17α-*Epoxy*-6α,16β-*dimethylpregn*-4-*ene*-3,20-*dione*** formed needles, m. p. 182—184°, $[\alpha]_D^{22}$ +130° (*c* 0·43), $\lambda_{max.}$ 239 mμ (log ε 4·22) (Found: C, 77·8; H, 9·0. $C_{23}H_{32}O_3$ requires C, 77·5; H, 9·0%).

17α-*Hydroxy*-6α-*methyl*-16-*methylenepregn*-4-*ene*-3,20-*dione* (V; R = Me, R′ = H, R″ = CH_2).—(*a*) 16α,17α-Epoxy-6,16β-dimethylpregn-4-ene-3,20-dione (4 g.), dissolved in glacial acetic at 10°, was treated, with stirring, with 4 ml. of a 50% w/v solution of hydrogen bromide in acetic acid. After 15 min. the mixture was poured into water. The product was extracted with ether and crystallised from methanol, to give **17α-*hydroxy*-6α-*methyl*-16-*methylenepregn*-4-*ene*-3,20-*dione***, needles, m. p. 212—214°, $[\alpha]_D^{21}$ −15° (*c*, 0·6), $\lambda_{max.}$ 239·5 mμ (ε 17,638) (Found: C, 77·2; H, 8·7. $C_{23}H_{32}O_3$ requires C, 77·5; H, 9·0%).

(*b*) Concentrated sulphuric acid (1 ml.) was added to a solution of 16α,17α-epoxy-6α,16β-dimethylpregn-4-ene-3,20-dione (10 g.) in dioxan (200 ml.). After being kept overnight at room temperature, the mixture was poured into water, and the precipitated solids were collected, washed with water, and crystallised from methanol, to give the preceding diketone, m. p. and mixed m. p. 210—214°.

3,17α-*Diacetoxy*-6-*methyl*-16-*methylenepregna*-3,5-*dien*-20-*one*.—The foregoing compound (V; R = Me, R′ = H, R″ = CH_2) (500 mg.) was dissolved in acetic acid (5 ml.) and acetic anhydride (2·5 ml.) containing toluene-*p*-sulphonic acid monohydrate (0·05 mg.). The mixture was left at room temperature for 24 hr., and then poured into ice and water. The dark brown precipitate was extracted with ether, and the ether extracts were washed with sodium hydrogen carbonate solution and water. The residue obtained by evaporation of the ether extracts was purified from methanol containing a few drops of pyridine. **3,17α-*Diacetoxy*-6-*methyl*-16-*methylenepregna*-3,5-*dien*-20-*one*** crystallised in plates, m. p. 148—149°, $[\alpha]_D^{25}$ −237° (*c* 0·8), $\lambda_{max.}$ 244 mμ (ε 18,400) (Found: C, 73·2; H, 8·27. $C_{27}H_{36}O_5$ requires C, 73·5; H, 8·2%).

17α-*Acetoxy*-6α-*methyl*-16-*methylenepregn*-4-*ene*-3,20-*dione* (V; R = Me, R′ = Ac, R″ = CH_2).—The foregoing diacetate (0·5 g.) was dissolved in methanol (100 ml.), and a solution of potassium hydroxide (0·5 g.) in water (2 ml.) and methanol (5 ml.) was added. After 10 min. acetic acid (1 ml.) was poured into the reaction mixture, which was then evaporated under reduced pressure to small volume and poured into water. The precipitated solids were purified from methanol, to give **17α-*acetoxy*-6α-*methyl*-16-*methylenepregn*-4-*ene*-3,20-*dione***, needles, m. p. 206—208°, $[\alpha]_D$ −98° (*c* 0·21), $\lambda_{max.}$ 240 mμ (ε 15,200) (Found: C, 75·0; H, 8·4. $C_{25}H_{34}O_5$ requires C, 75·2; H, 8·5%). An alternative preparation is described below.

3β-*Acetoxy*-6,16-*dimethylpregna*-5,14,16-*trien*-20-*one*.—3β-Acetoxy-16α,17α-epoxy-6,16β-dimethylpregn-5-en-20-one (10 g.) in glacial acetic acid (500 ml.) was treated at 0° with 15 ml. of a 50% w/v solution of hydrogen bromide in acetic acid with stirring. After 30 min. the mixture was poured into water. The precipitated solids were purified from methanol, to give **3β-*acetoxy*-6,16-*dimethylpregna*-5,14,16-*trien*-20-*one***, needles, m. p. 225—227°, $[\alpha]_D^{21}$ +282° (*c* 0·234), $\lambda_{max.}$ 309 mμ (ε 11,650), $\nu_{max.}$ (in CH_2Cl_2) 1729, 1627, 1534 cm.$^{-1}$ (Found: C, 78·4; H, 8·8. $C_{25}H_{36}O_3$ requires C, 78·2; H, 9·3%).

3β-*Acetoxy*-17α-*hydroxy*-6-*methyl*-16-*methylenepregn*-5-*en*-20-*one* (IV; R = Ac, R′ = H).—(*a*) 3β-Acetoxy-16α,17α-epoxy-6,16β-dimethylpregn-5-en-20-one (III; R = Ac) (20 g.) was dissolved in dioxan (200 ml.) and mixed with 10 ml. of a 50% w/v solution of hydrogen bromide in acetic acid. After 10 min. at room temperature, the mixture was poured into water. The product was extracted with ether. Crystallisation from hexane gave **3β-*acetoxy*-17α-*hydroxy*-6-*methyl*-16-*methylenepregn*-5-*en*-20-*one***, needles, m. p. 126—128° and 147—149°, $[\alpha]_D^{24}$ −161° (*c* 0·31) (Found: C, 74·7; H, 9·2. $C_{25}H_{36}O_4$ requires C, 75·0; H, 9·0%).

(*b*) Concentrated sulphuric acid (0·5 ml.) was added to a solution of 3β-acetoxy-16α,17α-epoxy-6,16β-dimethylpregn-5-en-20-one (5 g.) in tetrahydrofuran (100 ml.), and the mixture was left overnight at room temperature, then poured into water. The precipitated solids crystallised from hexane, to give 3β-acetoxy-17α-hydroxy-6-methyl-16-methylenepregn-5-en-20-one, m. p. and mixed m. p. 147—149°.

3β,17α-*Diacetoxy*-6-*methyl*-16-*methylenepregn*-5-*en*-20-*one* (IV; R = R′ = Ac).—(*a*) A solution of the 17α-hydroxy-derivative (IV; R = Ac, R′ = H) (5 g.) and toluene-*p*-sulphonic acid monohydrate (0·75 g.) in acetic anhydride (25 ml.) and acetic acid (50 ml.) was left at room temperature overnight and then poured into ice–water. The product was extracted with ether. It crystallised from hexane in two forms which were separated by hand: (i) clusters of yellow plates, m. p. 218—220°, shown by their infrared spectrum and mixed m. p. to be

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3β-acetoxy-6,16-dimethylpregna-5,14,16-trien-20-one, and (ii) 3β,17α-*diacetoxy*-6-*methyl*-16-*methylenepregn*-5-*en*-20-*one*, needles, m. p. 166—168°, $[\alpha]_D^{25}$ −178° (*c* 0·88) (Found: C, 73·2; H, 8·75. $C_{21}H_{38}O_5$ requires C, 73·3; H, 8·6%).

(*b*) 3β-Acetoxy-17α-hydroxy-6-methyl-16-methylenepregn-5-en-20-one (IV; R = Ac, R′ = H) (4 g.) and toluene-*p*-sulphonic acid monohydrate (600 mg.) were dissolved in acetic anhydride (40 ml.) and left at room temperature overnight, yielding, from hexane, 3β,17α-diacetoxy-6-methyl-16-methylenepregn-5-en-20-one, m. p. 166—168°, identical with the specimen described above.

17α-*Acetoxy*-3β-*hydroxy*-6-*methyl*-16-*methylenepregn*-5-*en*-20-*one* (IV; R = H, R′ = Ac).—The foregoing diacetate (IV; R = R′ = Ac) (5 g.) was heated under reflux in methanol (150 ml.) containing concentrated hydrochloric acid (3 ml.) for 90 min. The solution was concentrated under reduced pressure and poured into water, and the precipitated solids were collected. Crystallisation from aqueous methanol gave 17α-*acetoxy*-3β-*hydroxy*-6-*methyl*-16-*methylenepregn*-5-*en*-20-*one*, needles, m. p. 163—165°, $[\alpha]_D^{25}$ −165° (*c* 0·33) (Found: C, 74·8; H, 9·1. $C_{25}H_{36}O_4$ requires C, 75·0; H, 9·0%).

17α-*Acetoxy*-6α-*methyl*-16-*methylenepregn*-4-*ene*-3,20-*dione* (V; R = Me, R′ = Ac, R″ = CH_2).—17α-Acetoxy-3β-hydroxy-6-methyl-16-methylenepregn-5-en-20-one (IV; R = H, R′ = Ac) (5 g.) in dry cyclohexanone (60 ml.) was added to aluminium t-butoxide (5 g.) in dry toluene (40 ml.), and the mixture was heated under reflux for 45 min. The product was isolated with methylene chloride and purified from methanol, yielding 17α-acetoxy-6α-methyl-16-methylenepregn-4-ene-3,20-dione, needles, m. p. 208—210°, identical with a specimen prepared as described above.

3β-*Hydroxy*-6,16α-*dimethylpregn*-5-*en*-20-*one*.—3β-Acetoxy-6-methylpregn-5-en-20-one (II; R = H) (10 g.) in dry toluene (200 ml.) was added to a solution of methylmagnesium iodide prepared from magnesium (10 g.) and methyl iodide (40 g.) in dry ether (200 ml.). The mixture was heated and stirred and the ether distilled off until the vapour temperature reached 80°, then the mixture was heated under reflux for 8 hr. The Grignard complex was hydrolysed with ammonium chloride solution, and the product was extracted with ether. The residue of 3β-hydroxy-6,16α-dimethylpregn-5-en-20-one and 3β,20-dihydroxy-6-methylbisnorchola-5,16-diene was heated with semicarbazide hydrochloride (10 g.) and sodium acetate (10 g.) in water (50 ml.) and methanol (150 ml.) for 1 hr. and then poured into water. The precipitate was collected, dried, and heated under reflux in ether (1 l.) for 1 hr. The ether-insoluble material, which was the semicarbazone of the required compound, was heated on the steam-bath with pyruvic acid (5 ml.), acetic acid (35 ml.), sodium acetate (6 g.) and water (12 ml.) for 5 hr.; this mixture was then evaporated to dryness *in vacuo* and the residue extracted with ether; the ether extracts were washed with aqueous sodium hydrogen carbonate and water, dried, and evaporated; the residue crystallised from acetone–hexane, to give 3β-hydroxy-6,16α-dimethylpregn-5-en-20-one, m. p. 170—172°, $[\alpha]_D$ −6° (*c* 0·46) (Found: C, 79·9; H, 10·3. Calc. for $C_{23}H_{36}O_2$: C, 80·2; H, 10·5%) (Schneider and Murray [3] give m. p. 170—172°, $[\alpha]_D$ −5°). Acetylation with acetic anhydride–pyridine at 100° for 1 hr. gave 3β-*acetoxy*-6,16α-*dimethylpregn*-5-*en*-20-*one*, m. p. 135—137°, $[\alpha]_D$ −17° (*c* 0·80) (Found: C, 77·6; H, 10·1. $C_{25}H_{38}O_3$ requires C, 77·7; H, 9·8%).

6α,16α-*Dimethylpregn*-4-*ene*-3,20-*dione* (I; R = Me).—3β-Hydroxy-6,16α-dimethylpregn-5-en-20-one (4 g.) was dissolved in dry cyclohexanone (60 ml.), and the solution was distilled until 10 ml. of distillate had been collected. To this solution was added aluminium t-butoxide (4 g.) in dry toluene (32 ml.), and the mixture was heated under reflux for 45 min. The product was extracted with ether and crystallised from aqueous methanol, to give 6α,16α-dimethylpregn-4-ene-3,20-dione, needles, m. p. 120—122°, $\lambda_{max.}$ 241 mμ (ε 16,230), $[\alpha]_D^{23}$ +144° (*c* 1·12) (Found: C, 80·4; H, 10·0. Calc. for $C_{23}H_{34}O_2$: C, 80·6; H, 9·9%) {Graber and Meyers [4] give m. p. 122—126°, $[\alpha]_D$ +144°, $\lambda_{max.}$ 241 mμ (ε 15,450)}.

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[3] Schneider and Murray, *Chem. and Ind.*, 1960, 1163.
[4] Graber and Meyers, *Chem. and Ind.*, 1960, 1478.

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551. *A Quantitative Study of the Nitration of Benzothiazole.*

By E. R. Ward and W. H. Poesche.

The mononitration of benzothiazole in nitric–sulphuric acid, at 10° and 35°, has been quantitatively investigated. All four mononitrobenzothiazoles are produced, the 5-isomer being detected for the first time as a nitration product. The orientation of the four isomers has been unequivocally established, use being made of the relation between dipole moment and elution behaviour in chromatography on alumina as supporting evidence. A procedure is described for isolating the nitro-compounds in quantity.

In view of recent interest in benzothiazole it was surprising to find no comprehensive investigation of its mononitration. In 1883 Mylius [1] isolated 6-nitrobenzothiazole as a nitration product and established its structure by conversion into *p*-phenylenediamine. Later investigators have confirmed the 6-isomer as the major product but have made conflicting claims about the remainder. Nishizawa [2] claimed that he obtained, by nitration at room temperature or 60°, a quantitative yield, which he separated into 6-isomer and a supposed molecular compound (m. p. 138°) of the 6- and the 7-isomer, converted by catalytic reduction into the corresponding amines. However we have now shown that all four mononitro-derivatives are formed, with the 4- and the 7-isomer in about equal amount; the supposed molecular compound was shown by a mixed m. p. diagram not to exist, and the m. p. quoted for it does not correspond to that (m. p. 123°) of the eutectic mixture of 6- and 7-isomers; furthermore, 7-aminobenzothiazole had not been authenticated at the time.

Mizuno *et al.*[3] isolated the 6-isomer and what they presumed to be the 7-isomer. Peticolas *et al.*[4] isolated the 6-isomer and a small amount of a compound (m. p. 135°), which they presumed (possibly correctly) to be the 4-isomer. Veltman [5] was able to separate the nitration product by fractional crystallisation from methanol, ethanol, and benzene into 6-nitrobenzothiazole, 7-nitrobenzothiazole, and a substance, m. p. 106°, which he thought to be the 4-isomer, but which was obviously not pure, as can be seen from its low m. p. and the m. p. discrepancies of the derived amino- (123°) and 2-aminonitrobenzothiazole (235°) with those recorded for 4-amino- (94° [6]) and 2-amino-4-nitrobenzothiazole (254°,[6] 248° [7]).

We nitrated benzothiazole in nitric–sulphuric acid and from the product removed most of the predominant 6-isomer by means of solvent. The remainder was separated into its four components by column chromatography on alumina, using the technique that had been successful for separation of polynitronaphthalenes.[8] Our results are summarised in the Table.

Nitration of benzothiazole in sulphuric (*d* 1·84) *and nitric acid* (*d* 1·5).

		Product composition (%)			
Temp.	Yield (%) *	4-NO_2	5-NO_2	6-NO_2	7-NO_2
10° ± 2°	83	22·8	6·4	49·5	21·3
35° ± 2°	91·6	21·4	8·5	50·1	20·0

* Total yield of pure mononitrobenzothiazoles.

The nitro-compounds were eluted in the order 7-, 6-, 5-, 4-; good separation was

[1] Mylius, Dissertation, Berlin, 1883.
[2] Nishizawa, *J. Pharm. Soc. Japan*, 1942, **62**, 47.
[3] Mizuna, Adachi, and Nakamura, *J. Pharm. Soc. Japan*, 1952, **72**, 1266.
[4] Peticolas, Sureau, Frenkiel, and Goupil, *Bull. Soc. chim. France*, 1949, 111.
[5] Veltman, *J. Gen. Chem. U.S.S.R.*, 1960, **30**, 1363.
[6] Erlenmeyer and Ueberwasser, *Helv. Chim. Acta*, 1940, 328.
[7] Elderfield and Short, *J. Org. Chem.*, 1953, **18**, 1092.
[8] (*a*) Ward, Johnson, and Day, *J.*, 1959, 487; (*b*) Johnson, Thesis, London, 1960; (*c*) Ward and Johnson, *J.*, 1961, in the press.

achieved between the last three isomers but only partial separation between the 7- and the 6-isomer (see also the discussion below of the relation between dipole moment and elution behaviour). The composition of mixtures of 6- and 7-isomers was therefore determined from the mixed m. p. diagram (accuracy *ca.* ±1%). The accuracy of the chromatographic separations is estimated at ±2% but may be better. The absence of other isomers in the individual nitro-compounds or in the mixture of 6- and 7-isomers was confirmed by infrared spectroscopy.

The chromatographic method is not suitable for the preparation of the nitrobenzothiazoles in quantity, so we devised an alternative procedure. Most of the 6-isomer (*ca.* 85% of it) is readily obtained by simple solvent separation. The residue is steam-distilled, yielding a mixture (A) of the 6- and the 7-isomer, and a non-volatile residue (B) of the 4- and the 5-isomer. 7-Nitrobenzothiazole (*ca.* 55% of it) is obtained from mixture (A) by destruction of the 6-isomer with methanolic sodium hydroxide (cf. Mizuno [3]). Crystallisation of mixture (B) from methanol and then from xylene yields the 4-isomer (*ca.* 40%); and the 5-isomer (*ca.* 25%) can be obtained from the residue by destroying the 4-isomer as above; alternatively, but more laboriously, the 4- and the 5-isomer can be separated by column chromatography. The original steam-distillation is tedious owing to the low volatility of the 6- and the 7-isomer, and satisfactory separation by solvents only was impossible.

Before this work the orientation of the 5-isomer had been established by synthesis [9] and that of the 6-isomer by Mylius [1] and Colonna and Anderson.[10] The identity of our products with these, together with the orientation of the other isomers has been shown by melting points, infrared spectra, calculated and measured dipole moments, and the relation of the last to elution behaviour on alumina. The infrared spectra of all four isomers show peaks which can be allocated (*a*) to those considered by O'Sullivan [11] to be characteristic of a benzene ring fused to a five-membered ring, and (*b*) to the hydrogen ring patterns in the benzene ring [12] [801 cm.$^{-1}$ (hydrogen pattern 1,2,3) for the 4- and the 7-isomer; 813 cm.$^{-1}$ (5-) and 818 cm.$^{-1}$ (6-) (hydrogen pattern 1,2), 922 cm.$^{-1}$ (5-) and 899 cm.$^{-1}$ (6-) (hydrogen pattern 1) for the 5- and the 6-isomer].

With isomeric molecules, which contain the same number and same type of functional groups, the elution sequence in column chromatography is often indirectly proportional to the order of dipole moments for the compounds.[8,13] The elution order for the nitrobenzothiazoles was $7 \geqslant 6 > 5 > 4$. This order is consistent with the dipole moments calculated for these (7-nitro-, 2·3; 6-nitro-, 2·9; 5-nitro-, 4·8; 4-nitro-, 5·7 D). Further, the dipole moments of the 4- and the 7-isomer were measured by us, being about 5·2 and 2·5 D respectively, giving reasonable agreement with the calculated values. The dipole moments were calculated by using values of 4·0 D for the nitro-group and 1·45 D for benzothiazole.[14] The direction of the latter was derived by vector addition of the calculated π- and σ-moments of benzothiazole.[15] When the charge-density diagram of Metzger and Pullmann [16] and an " exageration factor " of 10/3 (calculated from the similarly obtained pyridine diagram) were used, the π-moment found was 2·41 D, θ 353½°. Using C–H + 0·40, C–N − 0·45, and a formal C–S moment of −1·0 D (calculated from the similarly obtained thiophen diagram) we found the σ-moment to be 1·02 D, θ 126½°. This gives a resultant angle of 18° (bisecting the C–N–C angle) for benzothiazole; the calculated magnitude of 1·87 D is in fair agreement with experiment, and shows that some reliance can be attached to the calculations. Further, the sequence of calculated dipole moments is not altered when

[9] Brand, *Z. angew. Chem.*, 1928, **41**, 614; Spieler and Prijs, *Helv. Chim. Acta*, 1950, **33**, 1429.
[10] Colonna and Andrisano (*Publ. Ist. chim. Univ. Bologna*, 1943, *No.* 3, 3; *Chem. Abs.*, 1947, **41**, 754).
[11] O'Sullivan, *J.*, 1960, 3278.
[12] Hawkins, Ward, and Whiffen, *Spectrochim. Acta*, 1957, **10**, 106.
[13] Franc and Latinak, *Coll. Czech. Chem. Comm.*, 1955, **20**, 817.
[14] Oesper, Lewis, and Smyth, *J. Amer. Chem. Soc.*, 1942, **64**, 1131.
[15] Orgel, Cottrell, Dick, and Sutton, *Trans. Faraday Soc.*, 1951, **47**, 113.
[16] Metzger and Pullmann, *Compt. rend.*, 1948, **226**, 1614.

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the direction of the benzothiazole moment is varied by ±15° (the accuracy claimed for the method of calculation [15] is ±10°).

Experimental

Dipole moments were measured by Dr. S. Walker and Mr. A. N. Sharpe, B.Sc., by the method described previously.[9] Ultraviolet spectra were recorded with a Unicam S.P. 500 spectrophotometer for cyclohexane solutions. The infrared spectra were measured for Nujol mulls by Dr. K. Morgan (University of Birmingham).

Nitration of Benzothiazole.—Benzothiazole (31·5 g.) was dissolved in sulphuric acid (*d* 1·84; 50 ml.) by portionwise addition, with vigorous stirring, below 20°. Nitric acid (*d* 1·5; 25 ml.) was added dropwise so that the temperature was maintained at 10° ± 2° (or 35° ± 2°), and this temperature was then maintained for a further hr. The mixture was poured on ice (250 g.) with stirring, and aqueous ammonia (*d* 0·88) added, below 25°, till the solids became slightly orange (pH 2). The solids were collected, washed by agitation with dilute aqueous ammonia and water, and dried at 80° *in vacuo*. Yields were 49 g. (10°) and 47 g. (35°).

Analysis of the Nitration Product.—The product obtained by nitration at 10° was crystallised from hot ethanol (700 ml.), and the solids obtained on cooling were again dissolved in hot ethanol [550 ml. recovered from the original filtrate (used to prevent possible losses of volatile material in concentration of this filtrate) plus 150 ml. of fresh solvent]. The inorganic residue (8·2 g.) was removed from the hot solution which was set aside to crystallise slowly. Filtration gave 6-nitrobenzothiazole, m. p. 177° (14·78 g.). The combined filtrates were evaporated to dryness and the residue was dried *in vacuo* at 120° (25·6 g.). A portion (2·0 g.) of this residue was passed in benzene (200 ml.)–light petroleum (b. p. 40—60°; 25 ml.) through an alumina (B.D.H.) column (90 × 2·5 cm.) prepared in a similar solvent. Elution was with this solvent mixture (1700 ml.), followed by benzene (200 ml.) and 9 : 1 v/v benzene–ethyl acetate (400 ml.). When the product front had nearly reached the bottom of the column, 20-ml. fractions were collected. These were each evaporated to dryness and quickly dried *in vacuo* at 80°. The separation was followed from the appearance, weights, and m. p.s of the recovered solids. The column was finally washed with ethanol but this only afforded by-products. Before the product front reached the base of the column the eluent contained only by-products (0·1160 g.). Fractions 1—10 also contained by-products (0·0838 g.). After this 7-nitrobenzothiazole began to appear (fractions 11—17), followed by a mixture of this with 6-nitrobenzothiazole (18—31) and finally almost pure 6-isomer (32—36) (fractions 11—36 contained 0·7464 g.). The next fraction (37) was pure eluent. 5-Nitrobenzothiazole was collected from fractions 38—50 (0·1712 g.), again followed by pure solvent (51—52). 4-Nitrobenzothiazole was in fractions 53—73 (0·6124 g.). The combined yield of nitrobenzothiazoles was 1·5300 g. The ethanol elution gave more by-products (0·1155 g.) (total recovery of solids 1·8453 g., *ca.* 92%).

The mixture of 6- and 7-nitrobenzothiazoles was analysed by mixed m. p. diagram, based on the following values:

6-Nitro-compd. (%)	0	10	20	30	35	40	60	70	100
M. p.	153°	147°	138°	128·5°	123°	126°	148°	157°	177°

The product obtained by nitration at 35° was analysed similarly.

Preparation of the Nitrobenzothiazoles.—The yields given below are the amount of each isomer recovered in relation to the total amount of this in the nitration product, as indicated by the chromatographic analysis. Almost pure 6-nitrobenzothiazole (m. p. 177°; *ca.* 83%) was obtained by crystallization from hot ethanol as described above. The product (30 g.) obtained by evaporation of the ethanol filtrates (containing *ca.* 8·3 g. of 7-, 4·2 g. of 6-, 3·1 g. of 5-, and 9·3 g. of 4-isomer; cf. Table) was steam-distilled. After being kept at 0° overnight the distillates were filtered, yielding a mixture of 6- and 7-nitrobenzothiazole (9·8 g., *ca.* 80%). This mixture was dissolved in warm methanol (700 ml.) and treated with a solution of sodium hydroxide (5 g.) in methanol (100 ml.) at 25° (cf. Mizuno [3]); stirring was continued for 4 hr., the mixture was kept overnight at 0°, and the solids were collected and washed with ethanol, affording almost pure 7-nitrobenzothiazole, m. p. 154—155° (4·6 g., *ca.* 55%). The products (9·4 g., *ca.* 76% calc. on 4- and 5-isomers) not volatile in steam were collected from the residual aqueous suspension after this had been kept overnight at 0°. They were dissolved in hot methanol (350 ml.) (charcoal), concentrated to 140 ml., and set aside to crystallise. The solid (4·65 g.;

m. p. 131—133°) that separated was crystallised from hot xylene (30 ml.; charcoal), yielding the 4-nitro-isomer (3·7 g., *ca.* 40%; m. p. 135°). The xylene filtrate was evaporated and the residue dissolved in the methanol filtrate. This was then stirred with a solution of sodium hydroxide (1 g.) in methanol (20 ml.) for 2 hr., and the solids were collected after being kept at 0° overnight (1·9 g.). 5-Nitrobenzothiazole (0·8 g., *ca.* 25%; m. p. 161°) was recovered from this material by chromatography on alumina (100 × 2·5 cm.) in benzene, elution being with benzene until the faintly reddish-brown band (due to this isomer) nearly reached the base of the column, and then with benzene–ethyl acetate (19 : 1 v/v).

The products had the following properties:

4-*Nitrobenzothiazole*, greenish needles (from xylene), m. p. 137°, discoloured in air (Found: C, 47·0; H, 2·3; N, 15·6. $C_7H_4N_2O_2S$ requires C, 46·6; H, 2·2; N, 15·5%). Dipole moment, 5·20 ± 0·05 D at 25° in C_6H_6. $\lambda_{max.}$ 234sh, 240sh, 280 mμ (ε 11,390, 10,640, 5830), $\nu_{max.}$ 1609m, 1559m, 1514s, 1450s, 1410s, 1344s, 1318s, 1286s, 1218m, 1193m, 1118m, 1076m, 974w, 869s, 863m, 804s, 801s, 758w, 746m, 735s, 720m, 681w, 663w cm.$^{-1}$.

5-Nitrobenzothiazole, yellowish needles (from xylene), m. p. 164° (Brand [9] gives 162°) (Found: C, 46·8; H, 2·0; N, 15·7%), $\lambda_{max.}$ 235, 240, 283, 319sh mμ (ε 22,970, 23,980, 8560, 860), $\nu_{max.}$ 1600m, 1570m, 1511s, 1470m, 1429m, 1421m, 1408m, 1348s, 1281m, 1258m, 1194w, 1143m, 1088w, 1053m, 1038m, 931m, 922m, 847m, 833m, 813m, 796m, 736m, 685w, 662w cm.$^{-1}$.

6-Nitrobenzothiazole, yellowish needles (from ethanol), m. p. 178° (Jacobson and Kwaysser [17] give 176—177°), $\lambda_{max.}$ 220, 228sh, 281, 316sh, 329sh mμ (ε 20,810, 19,500, 12,000, 3780, 2150), $\nu_{max.}$ 1603m, 1572m, 1542w, 1510s, 1481m, 1456m, 1436s, 1406m, 1396m, 1344s, 1336s, 1296s, 1291s, 1254m, 1200m, 1141w, 1126m, 1117s, 1034m, 906s, 899m, 851s, 847s, 818w, 800s, 749s, 746s, 716m, 656w cm.$^{-1}$.

7-Nitrobenzothiazole, white leaflets (from xylene), m. p. 155° (Found: C, 47·0; H, 2·2; N, 15·7%). Dipole moment 2·46 ± 0·05 D at 25° in C_6H_6. $\lambda_{max.}$ 231sh, 236, 304, 324sh, 340sh mμ (ε 11,420, 11,790, 6500, 5900, 2730), $\nu_{max.}$ 1616m, 1567m, 1528s, 1514s, 1487s, 1460m, 1407m, 1350s, 1317s, 1286m, 1218m, 1198m, 1186s, 1155m, 1096m, 1057m, 988w, 971w, 910w, 857s, 841s, 806m, 801m, 735s, 710m, 665w cm.$^{-1}$.

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LEICESTER COLLEGE OF TECHNOLOGY AND COMMERCE,
LEICESTER.

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[17] Jacobson and Kwaysser, *Annalen*, 1893, **277**, 244.

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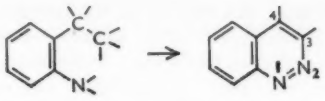
552. *A New Cinnoline Synthesis. Part I. Cyclisation of Mesoxalyl Chloride Phenylhydrazones to give Substituted 4-Hydroxycinnoline-3-carboxylic Acids.*

By H. J. BARBER, K. WASHBOURN, W. R. WRAGG, and (in part) E. LUNT.

A new and convenient synthesis of the cinnoline ring system starting from the readily accessible diethyl mesoxalate phenylhydrazones (I) is described. The products are 4-hydroxycinnoline-3-carboxylic acids (V), which on decarboxylation gave the corresponding 4-hydroxycinnolines (VI). Except for a single case, attempts to extend the scope of the synthesis to a wide variety of phenylhydrazones of type (VII) were unsuccessful.

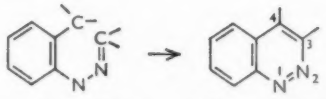
MOST known syntheses of the cinnoline ring system [1] involve the formation of the hetero-ring from benzene derivatives carrying an amino-group *ortho* to a suitably activated two-carbon chain. The additional nitrogen atom is introduced by a diazo-reaction and cyclisation takes place between the nitrogen atom and the carbon atom representing positions 2 and 3 respectively in the newly formed ring (Scheme A). These syntheses

[1] Simpson, "The Chemistry of Heterocyclic Compounds," Interscience Publ. Ltd., London, 1953, pp. 3—62; Alford and Schofield, *J.*, 1952, 2102.

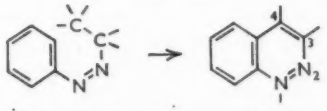
(A) 

depend on the availability of such starting materials as *o*-aminophenylpropiolic acids, *o*-aminoacetophenones, and *o*-aminophenylethylenes, very few of which are readily accessible.

A more recent synthesis [2] involves cyclisation between the carbon atoms which become positions 3 and 4 in the newly formed ring (Scheme B). Again the starting materials, *o*-acylphenylhydrazones, are relatively inaccessible.

(B) 

So far as we know no syntheses depending on cyclisation between the benzene ring and the carbon atom which becomes position 4 (Scheme C) have hitherto been described.

(C) 

The present series of papers describes the development of a novel synthesis of this type based on the Friedel–Crafts cyclisation of mesoxalyl chloride phenylhydrazones (IV) to derivatives of 4-hydroxycinnoline-3-carboxylic acids (V). An important feature of this route is the easy preparation, generally in excellent yield, of the starting materials—diethyl mesoxalate phenylhydrazones (I; see Table 1)—by coupling of diazotised aromatic amines with diethyl malonate in presence of sodium acetate.[3,4] Further, the yields at the subsequent stages often approach 90% and a very good overall yield is obtained. The reaction sequence is as in (I)—(V). We have adopted the phenylhydrazone rather than the tautomeric azo-structure for the products (I) in view of Bülow and Ganghöfer's chemical evidence,[5] Stevens and Ward's ultraviolet spectroscopic evidence,[6] and recent nuclear magnetic resonance studies.[7] In three cases the coupling reaction with diethyl malonate failed: 2,4-dinitrobenzenediazonium sulphate gave *m*-dinitrobenzene, *p*-dimethylaminobenzenediazonium chloride gave only an intractable tar, and from biphenyl-2-diazonium chloride the only product isolated was 2,2′-diazoaminobiphenyl. Most of the phenylhydrazones (I) separated in crystalline form after the coupling reaction; those which were liquid, with the exception of (I; R = *p*-OMe, R′ = H), distilled under a high vacuum and then crystallised.

The diesters (I) were best hydrolysed to the mesoxalic acid phenylhydrazones (III) in two steps. Treatment in boiling ethanol with sodium hydroxide (1 mol.) gave the relatively stable acid esters (II) rapidly and in high yield. Some of these intermediates (II) were isolated and characterised (Table 2). Usually, however, hydrolysis was completed *in situ* by reaction with further sodium hydroxide (2 mol.), normally at 50—80° but sometimes, to minimise decarboxylation and formation of by-products, at 18° (Table 3). Two diesters (I; R = *p*-OH, R′ = H; and R = *p*-O·CH_2Ph, R′ = H) underwent substantial decarboxylation during hydrolysis even at 25°, no diacid being obtained from the

[2] Baumgarten and de Brunner, *J. Amer. Chem. Soc.*, 1954, **76**, 3489; Baumgarten, Pedersen, and Hunt, *ibid.*, 1958, **80**, 1977; Baumgarten and Anderson, *ibid.*, p. 1981.
[3] Hantzsch and Thompson, *Ber.*, 1905, **38**, 2266.
[4] Meyer, *Ber.*, 1891, **24**, 1241.
[5] Bülow and Ganghöfer, *Ber.*, 1904, **37**, 4169.
[6] Stevens and Ward, *J.*, 1924, **125**, 1324.
[7] Anson, *Chem. and Ind.*, 1958, 1627.

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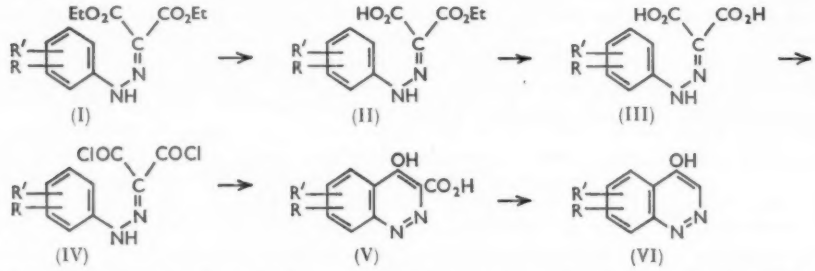
former, and only a low yield of diacid from the latter. Three further diacids (III; R = *p*-OMe, R′ = H; R = *p*-NHAc, R′ = H; and R = *p*-NH·CO_2Et, R′ = H) showed similar instability on attempted recrystallisation. By contrast, the diacids (III; R = *o*- and *p*-NO_2, R′ = H) were particularly stable, being recovered after prolonged boiling with dilute hydrochloric acid.



Mesoxalyl chloride phenylhydrazones (IV) have not previously been described. They proved to be moderately stable, crystalline, and easily prepared by heating the corresponding diacids (III) with a slight excess of thionyl chloride in an inert solvent, chosen so that the product crystallised on cooling. When reaction with thionyl chloride was sluggish, phosphorus pentachloride was used. The reaction failed in two cases; the diacid (III; R = *p*-NHAc, R′ = H) was recovered, whilst (III; R = *p*-NH·CO_2Et, R′ = H) gave only unidentified products. Three other diacids (III; R = 3-Br, R′ = 4-Me; R = *p*-OMe, R′ = H; and R = *o*-O·SO_2·C_6H_4Me-*p*, R′ = H) gave chlorides which could not be characterised but nevertheless gave the expected cinnoline derivatives on cyclisation.

The optimum conditions for cyclisation to the acids (V) (see Table 5) consisted in heating the chlorides (IV) with titanium tetrachloride (1·1 mol.) in nitrobenzene at 100° and hydrolysing the products with dilute alkali, but the parent mesoxalyl chloride phenylhydrazone (IV; R = R′ = H) was best cyclised in ethylene dichloride.

The cinnoline structure of the product obtained from the chloride (IV; R = *p*-Cl, R′ = H) was established by its identity with authentic 6-chloro-4-hydroxycinnoline-3-carboxylic acid, prepared from 5-chloro-2-nitrobenzaldehyde by a five-stage Richter synthesis.[8] [In following Schofield and Swain's preparative details we were unable to isolate the intermediate 5-chloro-2-nitrophenylpropiolic acid on dehydrobromination of αβ-dibromo-β-(5-chloro-2-nitrophenyl)propionic acid with aqueous-ethanolic sodium hydroxide at 25°, the only product being 5-chloro-2-nitrocinnamic acid; when the ethanol was omitted, the desired dehydrobromination proceeded smoothly at 40—45° in 73% yield.]

Further evidence for the cinnoline structure of our cyclisation products was that three of them (from the chlorides IV; R = R′ = H; R = *p*-Br, R′ = H; and R = *p*-Cl, R′ = H) melted at temperatures substantially the same as those reported for the expected 4-hydroxycinnoline-3-carboxylic acids (V) synthesised [8,9] by the Richter method. Moreover, when the 4-hydroxycinnoline-3-carboxylic acids (V) were decarboxylated in benzophenone [9] or Dowtherm at 200—215° to give the corresponding 4-hydroxycinnolines (VI; Table 6), two of the latter (VI; R = R′ = H; R = 6-NO_2, R′ = H) were identical with authentic samples prepared by the Borsche–Herbert synthesis.[10,11]

Three of the mesoxalyl chloride phenylhydrazones (IV; R = *m*-Cl, R′ = H; R = 3-Cl, R′ = 4-Cl; and R = 3-Br, R′ = 4-Me) which on cyclisation could theoretically

[8] Schofield and Swain, *J.*, 1949, 2393.
[9] Schofield and Simpson, *J.*, 1945, 512.
[10] Borsche and Herbert, *Annalen*, 1941, **546**, 293.
[11] Leonard and Boyd, *J. Org. Chem.*, 1946, **11**, 419.

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each give two isomers, gave in practice predominantly one isomer which was isolated pure in good yield. Structures were assigned (footnotes to Table 5) to two of these products; the orientation of the bromo-derivative was not determined.

The influence of reaction conditions on the cyclisation of mesoxalyl chloride phenylhydrazones (IV) was studied in some detail.

With the chloride (IV; R = *p*-Cl, R′ = H) in nitrobenzene at 95° very little cyclisation took place when 0·1 mol. of titanium tetrachloride was used as catalyst, and the yield and rate of reaction were not significantly improved by proportions of catalyst in excess of 1·1 mol. (behaviour typical of Friedel–Crafts acylation). Stannic chloride was as effective a catalyst as titanium tetrachloride for the cyclisation of both the chlorides (IV; R = R′ = H; and R = *p*-Cl, R′ = H), but often complete separation of the product from tin salts was very difficult. Moderate yields were obtained by using antimony pentachloride, anhydrous ferric chloride, or freshly sublimed aluminium chloride as catalyst for the cyclisation of the chloride (IV; R = *p*-Cl, R′ = H); these catalysts were unsuitable for the chloride (IV; R = R′ = H), intractable high-melting by-products being formed. Zinc chloride, silicon tetrachloride, phosphorus oxychloride, and the boron trifluoride–ether complex were ineffective as catalysts.

In the cyclisation of the chloride (IV; R = R′ = H) similar satisfactory yields were obtained by using ethylene dichloride, nitrobenzene, *sym*-tetrachloroethane, or chlorobenzene as solvent, but the first was preferred because the product separated as an insoluble crystalline complex. Isolation of a moderate yield when benzene was the solvent indicated that a polar solvent was not essential; on the other hand, no product was isolated on use of boiling toluene or tetralin at 95°. For other chlorides (IV) nitrobenzene was the preferred solvent.

In general, the optimum reaction temperature was 95—100°. For instance, although cyclisation of the chloride (IV; R = *p*-Cl, R′ = H) did not begin below 80°, a strongly exothermic reaction set in at 100°. Higher reaction temperatures were unsatisfactory; in fact, the starting material decomposed spontaneously in nitrobenzene above 130°.

Normally, the optimum reaction time was 4—6 hr., but in some difficult cases, for example, the cyclisation of the chloride (IV; R = 2-Cl, R′ = 4-Cl), the yield was significantly improved by longer heating.

After this successful use of mesoxalyl chloride phenylhydrazones (IV), attempts were made to extend the synthesis to the cyclisation of the corresponding glyoxylyl chlorides (VII; A = COCl, B = CO_2Et, H, CN, or NO_2). Of the intermediate glyoxylic esters (VII; A = CO_2Et, B = H, CN, or NO_2, R = H, *p*-Cl, or *p*-OMe), those where B = H were prepared from the corresponding mesoxalic acid esters (II) by decarboxylation, and those where B = CN or NO_2 were prepared from the appropriately substituted acetic esters by methods similar to that described for the diesters (I) (see Table 7). Except for the nitroglyoxylic esters (VII; A = CO_2Et, B = NO_2, R = H or *p*-Cl) which decomposed, the foregoing glyoxylic esters gave the corresponding glyoxylic acids on alkaline hydrolysis. These acids, together with the mesoxalic acid esters (II; R = *p*-Me, R′ = H; and R = *p*-O·CH_2Ph, R′ = H) were converted into the acid chlorides by a method similar to that used for the mesoxalyl chlorides (IV).

When the cyclisation of these acid chlorides was attempted under the previously determined optimum conditions, only the compound (VII; A = COCl, B = CO_2Et, R = *p*-Me) gave a cinnoline; instead of the expected ester (VIII; R = 6-Me), the product isolated was the corresponding acid (V; R = 6-Me, R′ = H) and owing to the presence of by-products the yield was low. This comparative lack of success may be due to the existence of these unsymmetrical phenylhydrazone monoacid chlorides in two stereoisomeric (*cis*- and *trans*-)forms, one of which has a configuration unfavourable to ring closure.

Further attempts to extend the reaction to a variety of phenylhydrazones of mesoxalic mono- and di-esters, acids, and nitriles, and to glyoxylic acids and esters, by using other established cyclisation methods were unsuccessful. Among the methods tried were

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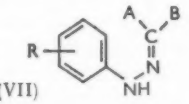
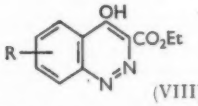
thermal cyclisation (cf. Leonard *et al.*[12]) of certain mesoxalic diesters (VII; A = B = CO_2Et and CO_2Me) and glyoxylic esters (VII; A = CO_2Et or CO_2Me, B = H), and treatment of mesoxalic and glyoxylic acids, esters, and nitriles (VII) with such reagents as concentrated sulphuric acid, concentrated sulphuric acid and acetic anhydride,[13] polyphosphoric acid, phosphorus oxychloride, anhydrous hydrofluoric acid, fluorosulphonic



(VII)



(VIII)

acid, and boron trifluoride–ether complex (Table 9). With sulphuric acid sulphonated starting material was sometimes obtained but, generally, either intractable by-products or unchanged material was isolated. In reactions of boron trifluoride–ether complex with the mesoxalic ester (I; R = *p*-Cl, R′ = H) crystalline boron-containing complexes were isolated that gave the corresponding mesoxalic acid ester (II; R = *p*-Cl, R′ = H) on treatment with acetic acid.

Experimental

o-*Benzyloxyaniline*.—*o*-Benzyloxynitrobenzene [14] (199 g.) in ethanol (2 l.) was hydrogenated in the presence of Adams catalyst (6 g.) at 40°/6 atm. Reduction required 4·5 hr. Evaporation and distillation gave *o*-benzyloxyaniline (162 g., 93·5%), b. p. 150—156°/0·1 mm., m. p. 37—39° (Sieglitz and Koch [15] give m. p. 39—40°).

o-*Aminophenyl Toluene*-p-*sulphonate*.—This was prepared similarly from the *o*-nitro-ester (384 g.) in ethanol (4 l.) over Adams catalyst (8 g.) at 6 atm. and a maximum temperature of 70°. Reduction was complete in 7·5 hr. After removal of the catalyst, the filtrate was concentrated; the amine (316 g., 93%) crystallised in buff plates, m. p. 97—98° (Bamberger and Rising [16] give m. p. 101°).

N-p-*Aminophenylurethane*.—*p*-Nitrophenylurethane (444 g.) in ethanol (2·5 l.) was similarly hydrogenated in the presence of Adams catalyst (4·4 g.) at room temperature and 20 atm. Reduction was complete in 40 min. After evaporation the residue was crystallised from benzene (500 ml.), giving *N*-*p*-aminophenylurethane (350 g., 92%) as a buff solid, m. p. 73—74° (Behrend [17] gives m. p. 73—74°).

Diethyl Mesoxalate Phenylhydrazones (I) (see Table 1).—In a typical preparation a slurry of *o*-chloroaniline hydrochloride made by adding molten *o*-chloroaniline (1·275 kg.) to concentrated hydrochloric acid (2·5 l.) was cooled to 0°, mixed with ice (5 kg.), and diazotised at 0—5° with sodium nitrite (705 g.) in water (1·67 l.). The filtered diazonium solution was added dropwise during 30 min. to a stirred mixture of diethyl malonate (1·6 l.), ethanol (20 l.), anhydrous sodium acetate (1·88 kg.), and water (3 l.) at 0°. Stirring was continued for 5 hr. while the temperature rose to 20°. The crystals were filtered off, washed with water (30 l.), and dried in air, giving a crude *product* (2·836 kg., 95%), m. p. 72—73°, suitable for use in the next stage.

Diethyl Mesoxalate p-*Hydroxyphenylhydrazone*.—Diethyl mesoxalate *p*-benzyloxyphenylhydrazone (52 g.) in ethanol (600 ml.) was hydrogenated in the presence of 10% palladised charcoal (10 g.) at 27° (max.)/5 atm. Reduction was complete in 7·5 hr. Evaporation and crystallisation of the residue from benzene–light petroleum (b. p. 60—80°) gave *diethyl mesoxalate* p-*hydroxyphenylhydrazone* (28·4 g.), m. p. 127—130°, which crystallised from ethylene dichloride in yellow prisms, m. p. 130—131° (Found: C, 55·7; H, 5·4; N, 10·3. $C_{13}H_{16}N_2O_5$ requires C, 55·7; H, 5·7; N, 10·0%).

Ethyl Hydrogen Mesoxalate Phenylhydrazones (II).—These esters are listed in Table 2. In a typical preparation 2N-sodium hydroxide (280 ml.) was added dropwise during 30 min. to a solution of ethyl mesoxalate *p*-tolylhydrazone (150 g.) in boiling ethanol (280 ml.), the mixture

[13] Leonard, Boyd, and Herbrandson, *J. Org. Chem.*, 1947, **12**, 47.
[13] Bangdiwala and Desai, *J. Indian Chem. Soc.*, 1953, **30**, 655.
[14] Kumpf, *Annalen*, 1884, **224**, 121.
[15] Sieglitz and Koch, *Ber.*, 1925, **58**, 78.
[16] Bamberger and Rising, *Ber.*, 1901, **34**, 241.
[17] Behrend, *Annalen*, 1886, **233**, 10.

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being kept just alkaline to phenolphthalein. The clear red solution was heated under reflux for a further 10 min. and then acidified at room temperature with 0·5N-hydrochloric acid. The precipitated ethyl hydrogen mesoxalate *p*-tolylhydrazone crystallised from ethanol (600 ml.) in yellow needles (88 g., 65%), m. p. 141° (decomp.).

Mesoxalic Acid Phenylhydrazones (III).—These compounds are listed in Table 3. In a typical experiment, the reaction was carried out in two stages as described.

Stage (1). 2N-Sodium hydroxide (4·8 l.) was added with stirring during 15 min. to diethyl mesoxalate *m*-chlorophenylhydrazone (2·3 kg.) in boiling ethanol (4·8 l.).

Stage (2). To the solution thus obtained N-sodium hydroxide (19·2 l.) was added and after being refluxed gently with stirring for 20 min. the solution was filtered (charcoal) into a stirred mixture of concentrated hydrochloric acid (2·9 l.) and water (8·7 l.) kept at 35—40° by addition of ice (15—20 kg.) as required. The yellow precipitate was filtered off, washed by resuspension in water, and crystallised from ethyl acetate, to give *mesoxalic acid* m-*chlorophenylhydrazone* (1·594 kg., 85%), m. p. 162—164° (decomp.), suitable for use in the next stage. For large-scale preparations ethyl acetate was the most convenient solvent for the diacids.

Mesoxalyl Chloride Phenylhydrazones (IV).—These *hydrazones* are listed in Table 4. In a typical experiment phosphorus pentachloride (10·025 kg.) was added to a stirred suspension of mesoxalic acid *o*-chlorophenylhydrazone (4·98 kg.) in dry chloroform (16·25 l.) at room temperature. (Table 4 specifies the reagent and solvent used for each preparation.) After the initial vigorous reaction had subsided, the mixture was heated under reflux for 1·5 hr. The *product* (4·78 kg.), m. p. 126—128° (decomp.), which separated when the mixture was cooled in ice was washed with dry light petroleum (b. p. 60—80°). After being dried *in vacuo* over silica gel it was suitable for use in the cyclisation stage.

5-Chloro-2-nitrophenylpropiolic acid (cf. Schofield and Swain [8]).—Powdered αβ-dibromo-β-(5-chloro-2-nitrophenyl)propionic acid (10 g.) was added to stirred 10% aqueous sodium hydroxide (40 ml.), and the mixture warmed at 40—45° until a clear solution was obtained. After being kept at room temperature for 3 hr., the solution was poured into 2N-sulphuric acid (50 ml.). Crystallisation of the precipitate from 2N-acetic acid gave 5-chloro-2-nitrophenylpropiolic acid (5·0 g.), colourless needles, m. p. 135° (decomp.) [Schofield and Swain [8] give m. p. 138° (decomp.)].

4-Hydroxycinnoline-3-carboxylic Acids (V).—These are listed in Table 5. In a typical experiment titanium tetrachloride (1·975 l.) was added, with stirring, to mesoxalyl chloride *o*-chlorophenylhydrazone (4·78 kg.) suspended in dry nitrobenzene (27·5 l.) in a glass-lined vessel. After the initial exothermic reaction, during which the temperature was kept below 100° by external cooling, the vessel was heated at 95° for 6 hr. (until the evolution of hydrogen chloride ceased). Sodium hydroxide (5·5 kg.) in water (69 l.) was then added and the nitrobenzene removed by steam-distillation. The residual solution was filtered (Hyflo Supercel) and the solid extracted with hot water (2 × 40 l.). Acidification of the combined filtrates gave a crude product which was purified by dissolution in 2N-ammonia (45 l.), filtration (Hyflo; charcoal), and reprecipitation, giving *8-chloro-4-hydroxycinnoline-3-carboxylic acid* (3·464 kg., 90%), m. p. 247—248° (decomp.). The *compounds* listed in Table 5, with the exception of those detailed below, were prepared in a similar way. In several cases the preparations were carried out in good yield on a 3—5 kg. scale. The yields of pure cinnoline were somewhat lower where separation of two possible isomers was involved, but the low yields in the case of 5,8- and 6,8-dichloro-4-hydroxycinnoline-3-carboxylic acid, even after long heating, were most surprising. The 6-methoxy-derivative was obtained in a satisfactory crude yield but was difficult to purify, whilst the 8-methoxy-isomer could be isolated pure only in low yield after repeated extraction with concentrated hydrochloric acid of an intractable high-melting acidic solid which was the major product (45%). Attempts to cyclise mesoxalyl chloride *o*-benzyloxyphenylhydrazone were unsuccessful, whilst the *o*-toluene-*p*′-sulphonyloxy-analogue gave only 6% of the corresponding cinnoline carboxylic acid.

As expected, substitution of the phenylhydrazone group by nitro exerted a deactivating effect, 6- and 8-nitro-4-hydroxycinnoline-3-carboxylic acid being obtained in only 20% and 12% yield, respectively.

4-Hydroxycinnoline-3-carboxylic Acid.—Titanium tetrachloride (420 ml.) was added during 20 min. to mesoxalyl chloride phenylhydrazone (858 g.) in dry ethylene dichloride (3·5 l.). When the initial vigorous reaction had subsided the solution was refluxed on the steam-bath for 7 hr. After removal of the solvent under reduced pressure, the solid residue was powdered

TABLE 1. *Diethyl mesoxalate phenylhydrazones* (I).

R	R′	Form	M. p.	Yield [a] (%)	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
H	H	Plates [a]	33—34° [b]	95	$C_{13}H_{16}N_2O_4$	59·4	6·15	11·0	—	59·1	6·1	10·6	—
o-Me	H	Needles [a]	89—90	76	$C_{14}H_{18}N_2O_4$	60·8	6·6	10·3	—	60·4	6·5	10·1	—
p-Me	H	Needles [a]	32—33 [f]	62	$C_{14}H_{18}N_2O_4$	60·6	6·5	10·4	—	60·4	6·5	10·1	—
o-Cl	H	Plates [b]	76—77	96	$C_{13}H_{15}ClN_2O_4$	—	—	9·5	11·9	—	—	9·4	11·9
m-Cl	H	Prisms [b]	57—58 [j]	77	$C_{13}H_{15}ClN_2O_4$	52·0	5·1	9·5	11·9	52·3	5·0	9·4	11·9
p-Cl	H	Needles [b]	76	76	$C_{13}H_{15}ClN_2O_4$	—	—	9·6	12·0	—	—	9·4	11·9
2-Cl	3-Cl	Plates [c,g]	96—97	96	$C_{13}H_{14}Cl_2N_2O_4$	—	—	8·4	21·1	—	—	8·4	21·3
2-Cl	4-Cl	Plates [b,g]	92	63	$C_{13}H_{14}Cl_2N_2O_4$	46·9	4·4	8·7	—	46·9	4·2	8·4	—
2-Cl	5-Cl	Needles [c]	90—92	77	$C_{13}H_{14}Cl_2N_2O_4$	—	—	8·3	21·3	—	—	8·4	21·3
3-Cl	4-Cl	Needles [b]	80—81	74	$C_{13}H_{14}Cl_2N_2O_4$	—	—	8·5	21·5	—	—	8·4	21·3
p-Br	H	Needles [b]	73 [k]	62	$C_{13}H_{15}BrN_2O_4$	—	—	—	—	—	—	—	—
3-Br	4-Me	Prisms [b]	73	68	$C_{14}H_{17}BrN_2O_4$	47·1	4·6	8·2	—	47·1	4·8	7·8	—
o-OMe	H	Needles [c]	56—57	88	$C_{14}H_{18}N_2O_5$	56·9	6·2	9·7	—	57·2	6·1	9·5	—
p-OMe	H	Needles [a]	38 [i]	47 [m]	$C_{14}H_{18}N_2O_5$	56·8	6·2	9·3	—	57·2	6·1	9·5	—
o-O·CH_2Ph	H	Needles [c,r]	76—78	74	$C_{20}H_{22}N_2O_5$	65·2	6·0	7·8	—	64·9	5·9	7·6	—
p-O·CH_2Ph	H	Needles [b]	73—74	69	$C_{20}H_{22}N_2O_5$	65·5	6·0	8·0	—	64·9	5·9	7·6	—
o-OTos [p]	H	Prisms [b]	106	72	$C_{22}H_{22}N_2O_7S$	55·4	5·1	6·7	—	55·3	5·1	6·5	—
o-NO_2	H	Needles [b]	77—78 [n]	91 [m]	$C_{13}H_{15}N_3O_6$	50·6	5·0	13·6	—	50·5	4·9	13·6	—
p-NO_2	H	Plates [d,g]	79—82 [o]	82 [m]	$C_{13}H_{15}N_3O_6$	—	—	—	—	—	—	—	—
p-NHAc	H	Plates [e]	156—157	56	$C_{15}H_{19}N_3O_5$	55·6	5·9	13·0	—	56·1	5·9	13·1	—
p-NH·CO_2Et	H	Prisms [b]	186—187	75	$C_{16}H_{21}N_3O_6$	54·7	6·0	12·1	—	54·7	6·0	12·0	—

[a] From light petroleum (b. p. 40—60°). [b] From ethanol. [c] From light petroleum (b. p. 60—80°). [d] From ethyl acetate–light petroleum (b. p. 60—80°). [e] From benzene. [f] Crystalline form and m. p. of a pure sample; yellow unless otherwise stated. [g] Yield of product sufficiently pure for use at next stage; normally the total yield of solid from the coupling reaction or in the case of liquid products, the total yield after stripping off excess of diethyl malonate *in vacuo*. [h] B. p. 145—150°/0·2 mm.; isolated as an oil by Hantzsch and Thompson,[3] but not characterised. [i] B. p. 135—136°/0·05 mm.; Staudinger and Hammet (*Helv. Chim. Acta*, 1921, **4**, 217) give m. p. 77°. [j] Leonard, Boyd, and Herbrandson [12] give m. p. 56°. [k] Hantzsch and Thompson [3] give m. p. 76°. [l] B. p. 160—175°/0·1 mm. with steady decomposition of undistilled product. [m] Coupling reaction carried out in water instead of in aqueous alcohol. [n] Fries, Franke, and Bruns (*Annalen*, 1934, **511**, 241) give m. p. 74°. [o] Hünig and Boes (*ibid.*, 1953, **579**, 28) give m. p. 81°. [p] Tos = *p*-$C_6H_4Me·SO_2$ here and in subsequent Tables. [q] Orange. [r] Brown.

TABLE 2. *Ethyl hydrogen mesoxalate phenylhydrazones* (II).

R	R′	Form [a]	M. p. [a] (decomp.)	Yield [f] (%)	Formula	Found (%) C	H	N	Hal	Required (%) C	H	N	Hal
H	H	Needles [b]	112—114° [g]	62	$C_{11}H_{12}N_2O_4$	—	—	—	—	—	—	—	—
p-Me	H	Needles [b]	141 [h]	65 [i]	$C_{12}H_{14}N_2O_4$	57·8	5·6	11·2	—	57·6	5·6	11·2	—
p-Cl	H	Needles [b]	167	47	$C_{11}H_{11}ClN_2O_4$	—	—	10·4	13·3	—	—	10·4	13·1
p-Br	H	Needles [d]	177—179	13 [j]	$C_{11}H_{11}BrN_2O_4$	—	—	9·1	25·0	—	—	8·9	25·4
p-OMe	H	Needles [b]	122—123	42	$C_{12}H_{14}N_2O_5$	54·1	5·2	10·8	—	54·1	5·3	10·5	—
p-O·CH_2Ph	H [k]	Needles [b]	122—123	97	$C_{18}H_{18}N_2O_5$	63·3	5·4	8·4	—	63·2	5·3	8·2	—
p-NO_2	H	Prisms [a,l]	201—202	66	$C_{11}H_{11}N_3O_6$	46·8	3·6	15·3	—	47·0	3·9	15·0	—
p-NHAc	H	Needles [b]	187	87	$C_{13}H_{15}N_3O_5$	53·0	4·8	14·3	—	53·2	5·1	14·3	—
p-NH·CO_2Et	H	Plates [b]	166—167	77	$C_{14}H_{17}N_3O_6$	51·7	5·1	13·4	—	52·0	5·3	13·0	—

[a] From 2-ethoxyethanol. [b] From ethanol. [c] From methanol. [d] From acetic acid. [e] Crystalline form and m. p. of a pure sample; yellow unless otherwise stated. [f] Yield of pure product. [g] Hantzsch and Thompson [3] give m. p. 115°. [h] von Pechmann (*Ber.*, 1894, **27**, 1679) gives m. p. 139·5°. [i] When hydrolysis was carried out in methanol instead of ethanol, transesterification occurred, the product being *methyl hydrogen mesoxalate* p-*tolylhydrazone* (50%), yellow prisms, m. p. 152—153° (decomp.) (from ethanol) (Found: C, 55·8; H, 5·1; N, 11·8; OMe, 13·0. $C_{11}H_{12}N_2O_4$ requires C, 55·9; H, 5·1; N, 11·9; OMe, 13·2%); mixed m. p. with authentic sample undepressed. [j] Isolated as a by-product, less soluble in ethanol than the corresponding mesoxalic acid phenylhydrazone (III; R = *p*-Br, R′ = H) in a preparation of the latter, in which the reaction time (10 min.) at 80° was too short. [k] Formed a very insoluble *sodium*, m. p. 168—170° (Found: N, 7·5; Na, 6·4. $C_{18}H_{17}N_2NaO_6$ requires N, 7·7; Na, 6·2%), and *potassium salt*, m. p. 239—240° (Found: K, 9·7; N, 6·9. $C_{18}H_{17}KN_2O_6$ requires K, 10·3; N, 7·4%). [l] Orange.

H, 5·1; N, 11·9; OMe, 13·2%); mixed m. p. with authentic sample undepressed. [j] Isolated as a by-product, less soluble in ethanol than the corresponding mesoxalic acid phenylhydrazone (III; R = *p*-Br, R′ = H) in a preparation of the latter, in which the reaction time (10 min.) at 80° was too short. [k] Formed a very insoluble *sodium*, m. p. 168—170° (Found: N, 7·5; Na, 6·4. $C_{18}H_{17}N_2NaO_6$ requires N, 7·7; Na, 6·2%), and *potassium salt*, m. p. 239—240° (Found: K, 9·7; N, 6·9. $C_{18}H_{17}KN_2O_6$ requires K, 10·3; N, 7·4%). [l] Orange.

TABLE 3. *Mesoxalic acid phenylhydrazones* (III).

R	R′	Condns. for 2nd stage Temp.	Time (min.)	M. p.[a]	Yield[b] (%)	Formula	Found (%) C	H	N	Hal	Required (%) C	H	N	Hal
H	H	18°	150	162—163°[c]	97[a]	$C_9H_8N_2O_4$								
o-Me	H	70—80	15	181—182[j]	97[b]	$C_{10}H_{10}N_2O_4$	54·6	5·0	12·8	—	54·1	4·5	12·6	—
p-Me	H	50	15	169—170[k]	67[a]	$C_{10}H_{10}N_2O_4$	54·4	4·7	12·5	—	54·1	4·5	12·6	—
o-Cl	H	70—80	15	178—179[l]	90[c,cq]	$C_9H_7ClN_2O_4$	44·8	3·0	11·7	15·0	44·5	2·9	11·5	14·6
m-Cl	H[r]	70—80	15	170	85[c]	$C_9H_7ClN_2O_4$	—	—	11·6	14·7	—	—	11·5	14·6
p-Cl	H	70—80	15	186—187[m]	68[c]	$C_9H_7ClN_2O_4$	—	—	11·5	14·4	—	—	11·5	14·6
2-Cl	3-Cl	70—80	15	200—202	83[c]	$C_9H_6Cl_2N_2O_4$	—	—	10·2	26·0	—	—	10·1	25·7
2-Cl	4-Cl	70—80	15	177—178[n]	83[a,u]	$C_9H_6Cl_2N_2O_4$	—	—	—	—	—	—	—	—
2-Cl	5-Cl	70—80	15	210—211	86[c,v]	$C_9H_6Cl_2N_2O_4$	—	—	10·0	25·5	—	—	10·1	25·7
3-Cl	4-Cl	70—80	10—15	185—186	60[c]	$C_9H_6Cl_2N_2O_4$	—	—	10·2	25·8	—	—	10·1	25·7
p-Br	H[s]	70—80	10	191—193[o]	74[c]	$C_9H_7BrN_2O_4$	38·0	2·5	9·8	—	37·6	2·4	9·8	—
3-Br	4-Me	70—80	10	187—188	48[c,w]	$C_{10}H_9BrN_2O_4$	39·7	3·0	9·5	26·8	39·9	3·0	9·3	26·6
o-OMe	H	60—65	15	159	92[c]	$C_{10}H_{10}N_2O_5$	50·5	4·0	11·6	—	50·4	4·2	11·8	—
p-OMe	H	18	180	140—142[ab]	43[a,cc,y]	$C_{10}H_{10}N_2O_5$	50·7	4·1	12·0	—	50·4	4·2	11·8	—
o-O·CH_2Ph	H	60—65	15	154—155	88[c]	$C_{16}H_{14}N_2O_5$	61·2	3·9	9·1	—	61·1	4·5	8·9	—
p-O·CH_2Ph	H	60—65	30	153—154	45[c,z]	$C_{16}H_{14}N_2O_5$	60·9	4·5	9·1	—	61·1	4·5	8·9	—
o-OTos	H	70—80	10	175	66[a]	$C_{16}H_{14}N_2O_7S$	51·1	4·0	—	S 8·4	50·8	3·7	—	S 8·5
o-NO_2	H	70—80	10	195—197[p]	72[d,ad]	$C_9H_7N_3O_6$	42·4	2·4	16·4	—	42·7	2·8	16·6	—
p-NO_2	H[t]	70—80	10—15	199—200[q]	92[c,ae]	$C_9H_7N_3O_6$	42·8	3·3	16·9	—	42·7	2·8	16·6	—
p-NHAc	H	35	25	180—181	90[f,x]	$C_{11}H_{11}N_3O_5$	49·3	4·2	15·6	—	49·8	4·2	15·9	—
p-NH·CO_2Et	H	18	210	175—176	55[a,aa,af]	$C_{12}H_{13}N_3O_6$	49·0	4·5	14·0	—	48·8	4·4	14·2	—

[a] From ethanol. [b] From aqueous ethanol. [c] From acetic acid. [d] From ethyl acetate. [e] From 2-ethoxyethanol. [f] From water. [g] Chattaway and Harris (*J.*, 1922, **121**, 2703), who prepared the diacids from sodium mesoxalate and the substituted phenylhydrazines found that the m. p. varied with the rate of heating over a range of about 8°. The m. p.s recorded above were obtained by heating the sample to 5° below its m. p. in 5 min., then at 5°/min. [h] Yield of product sufficiently pure for use at the next stage, normally after one crystallisation from the solvent specified; yellow needles unless otherwise specified. [i] Meyer [4] gives m. p. 163—164°. [j–o] Chattaway and Harris (*loc. cit.*) give m. p. [j] 163·5—172°, [k] 170·5—178°, [l] 175—182°, [m] 186·5—193°, [n] 182·5—188°, [o] none. [p] Fries, Franke, and Bruns (*Annalen*, 1934, **511**, 241) give m. p. 192°. [q] Auwers and Müller (*ibid.*, 1923, **434**, 165) give m. p. 202°. [r] For diester see Leonard, Boyd, and Herbrandson.[12] [s] For diester see Hantzsch and Thompson.[3] [t] For diester see Hünig and Boes (*Annalen*, 1953, **579**, 28). [u] Precipitation with N-hydrochloric acid, even at 80°, gave the insoluble disodium salt, converted into the diacid only by stirring with 2N-hydrochloric acid at 85° for 2 hr. [v] Precipitated by addition of hot concentrated hydrochloric acid to hot reaction mixture. [w] No attempt made to obtain optimum yield. [x] Attempts to improve the yield by using more forcing conditions led to isolation of *glyoxylic acid* p-*benzyloxyphenylhydrazone*, m. p. 115—116° (decomp.) (from ethanol) (Found: C, 67·2; H, 5·4; N, 10·2. $C_{15}H_{14}N_2O_3$ requires C, 66·8; H, 5·2; N, 10·3%). [y] Low yield due to partial decarboxylation during crystn. [z] Crude yield; partial decarboxylation made crystallisation on more than 2-g. scale impracticable. [aa] Also 29% diester recovered; insolubility and instability of diacid make crystallisation on more than 2-g. scale impracticable. [ab] Decomp. [ac] Red. [ad] Orange prisms. [ae] Buff. [af] Orange rhombs. [ag] Prisms.

TABLE 4. *Mesoxalyl chloride phenylhydrazones* (IV).

R	R′	Solvent	Reagent	M. p.[a] (decomp.)	Yield [b] (%)	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
H	H[m]	$CHCl_3$	$SOCl_2$	132—135° [c]	86	$C_9H_6Cl_2N_2O_2$	44·5	2·7	11·5	28·8	44·1	2·5	11·4	29·0
o-Me	H	$C_2H_4Cl_2$ [c]	PCl_5	145—147 [c]	86	$C_{10}H_8Cl_2N_2O_2$	—	—	10·8	27·3	—	—	10·6	27·4
p-Me	H	$CHCl_3$	PCl_5	143—144 [g]	71	$C_{10}H_8Cl_2N_2O_2$	46·7	3·4	10·7	26·2	46·3	3·1	10·6	27·4
o-Cl	H	$CHCl_3$	PCl_5	129—130 [c]	83	$C_9H_5Cl_3N_2O_2$	—	—	10·3	38·3	—	—	10·0	38·1
m-Cl	H	CCl_4	PCl_5	123—124 [g]	89	$C_9H_5Cl_3N_2O_2$	39·2	2·3	10·1	—	38·6	1·8	10·0	—
p-Cl	H [m]	$C_2H_4Cl_2$ [c]	PCl_5	156—157 [g]	89 [j]	$C_9H_5Cl_3N_2O_2$	—	—	10·3	38·0	—	—	10·0	38·1
2-Cl	3-Cl	CCl_4	PCl_5	103—104 [g]	83	$C_9H_4Cl_4N_2O_2$	—	—	9·0	45·2	—	—	8·9	45·2
2-Cl	4-Cl	$CHCl_3$	PCl_5	145—146 [h]	58	$C_9H_4Cl_4N_2O_2$	—	—	9·0	43·5	—	—	8·9	45·2
2-Cl	5-Cl	CCl_4	PCl_5	110—111 [c]	50	$C_9H_4Cl_4N_2O_2$	—	—	9·1	45·7	—	—	8·9	45·2
3-Cl	4-Cl	$CHCl_3$	$SOCl_2$	149—150 [g]	63	$C_9H_4Cl_4N_2O_2$	—	—	8·9	44·6	—	—	8·9	45·2
p-Br	H	$CHCl_3$	PCl_5	158—160 [g]	62	$C_9H_5BrCl_2N_2O_2$	—	—	9·0	47·0 [d]	—	—	8·6	46·6 [d]
o-OMe	H	C_6H_6	$SOCl_2$	172—173 [g]	83	$C_{10}H_8Cl_2N_2O_2$	—	—	10·4	24·9	—	—	10·2	25·8
o-O·CH_2Ph	H	$CHCl_3$	$SOCl_2$	142—143 [f,k]	98	$C_{16}H_{12}Cl_2N_2O_2$	53·7	3·7	7·9	22·6	54·7	3·4	8·0	20·2
p-O·CH_2Ph	H	$CHCl_3$	PCl_5	121—123 [g]	32	$C_{16}H_{12}Cl_2N_2O_2$	55·0	3·8	8·3	—	54·7	3·4	8·0	—
o-OTos	H	C_6H_6	PCl_5	121—123 [g,k]	90	$C_{16}H_{12}Cl_2N_2O_4S$	47·1	3·1	—	15·1	46·3	2·9	—	17·1
o-NO_2	H	$CHCl_3$	PCl_5	135—137 [g]	83	$C_9H_5Cl_2N_3O_4$	—	—	14·3	24·1	—	—	14·5	24·5
p-NO_2	H	C_6H_6	PCl_5	155—156 [c]	86	$C_9H_5Cl_2N_3O_4$	37·9	2·0	14·7	23·6	37·2	1·7	14·5	24·5

[a] M. p. of a pure sample, unless otherwise specified. [b] Yield of product sufficiently pure for use in the next stage. [c] Ethylene dichloride. [d] Total halogen as silver halide. [e] Yellow prisms. [f] Yellow prisms and plates. [g] Yellow needles. [h] Yellow plates. [i] Di-acid described by Meyer.[4] [j] Yield 83% in nitrobenzene. [k] A pure sample was not obtained. [l] Anilide, m. p. 174° (from ethanol) (Found: C, 70·5; H, 5·3; N, 15·7. Calc. for $C_{21}H_{18}N_4O_2$: C, 70·5; H, 5·0; N, 15·7%). Naik, Trivedi, and Mehta (*J. Indian Chem. Soc.*, 1943, **20**, 365) give m. p. 175°. [m] *Anilide*, m. p. 215° (from benzene) (Found: C, 64·3; H, 4·5; N, 14·55. $C_{21}H_{17}ClN_4O_2$ requires C, 64·2; H, 4·3; N, 14·3%).

TABLE 5. *4-Hydroxycinnoline-3-carboxylic acids* (V).

R	R′	Colour [a]	M. p.[a] (decomp.)	Yield (%)	Formula	Found (%) C	H	N	Hal	Required (%) C	H	N	Hal
H	H	Fawn [d]	267—268° [e]	77	$C_9H_6N_2O_3$	57·0	3·7	14·7	—	56·8	3·2	14·7	—
8-Me	H	Colourless [d]	263—264	92	$C_{10}H_8N_2O_3$	58·6	4·1	13·7	—	58·8	3·9	13·7	—
6-Me	H	Fawn [e]	269	87	$C_{10}H_8N_2O_3$	58·6	4·4	13·6	—	58·8	3·9	13·7	—
8-Cl	H	Fawn [d,p]	247—248	90	$C_9H_5ClN_2O_3$	48·2	2·5	12·4	—	48·1	2·2	12·5	—
5-Cl	H [b]	Silvery [e,p]	263—264	63	$C_9H_5ClN_2O_3$	48·3	2·5	12·2	15·8	48·1	2·2	12·5	15·8
6-Cl	H	Colourless [e]	267 [f]	96	$C_9H_5ClN_2O_3$	48·5	2·5	—	15·9	48·1	2·2	—	15·8
7-Cl	8-Cl	Colourless [e,q]	249—250	68 [g]	$C_9H_4Cl_2N_2O_3$	41·8	1·9	11·1	27·8	41·7	1·55	10·8	27·4
6-Cl	8-Cl	Fawn [d]	250—251	27 [g]	$C_9H_4Cl_2N_2O_3$	41·9	1·6	10·8	27·2	41·7	1·55	10·8	27·4
5-Cl	8-Cl	Fawn [d]	248—249	11	$C_9H_4Cl_2N_2O_3$	—	—	10·7	27·2	—	—	10·8	27·4
5-Cl	6-Cl [i]	Fawn [d]	268	46	$C_9H_4Cl_2N_2O_3$	42·1	2·2	10·5	—	41·7	1·55	10·8	—
6-Br	H	Yellow [e]	256—258 [h]	83	$C_9H_5BrN_2O_3$	—	—	—	—	—	—	—	—
5(or 7)-Br	6-Me [m]	Fawn [e]	262—263	40 [m]	$C_{10}H_7BrN_2O_3$	42·6	2·8	10·5	29·0	42·4	2·5	9·9	28·3
8-OMe	H	Pink [d]	274—275	16	$C_{10}H_8N_2O_4$	54·7	3·9	12·8	—	54·55	3·6	12·7	—
6-OMe	H	Fawn [d]	258—259 [j]	76	$C_{10}H_8N_2O_4$								
8-OTos	H	Colourless [d]	255	5	$C_{16}H_{12}N_2O_6S$	53·2	3·6	8·8	—	53·3	3·3	8·9	—
8-NO_2	H	Pale green [d,p]	253—254	12	$C_9H_5N_3O_5$	46·0	2·4	17·8	—	45·95	2·1	17·9	—
6-NO_2	H	Yellow [d]	275	20	$C_9H_5N_3O_5$	46·1	2·2	17·9	—	45·95	2·1	17·9	—

[a] M. p. of pure sample. [b] Obtained from cyclisation of (IV; R = *m*-Cl, R′ = H), after one crystallisation of the crude product from dimethyl formamide. Assigned structure based on the fact that the decarboxylated product and two derivatives, *5-chloro-4-phenoxycinnoline* and *4-amino-5-chlorocinnoline* had m. p.s different from those reported for the corresponding 7-chloro-isomers (see below and Table 6). [c] Schofield and Simpson [3] give m. p. 268—268·5° (decomp.). [d] From acetic acid. [e] From dimethylformamide. [f] This m. p. was undepressed in admixture with authentic sample (prepared as described by Schofield and Swain [8]), m. p. 267° (lit., 263—264°). [g] Reaction time 21 hr. [h] Schofield and Swain [8] give m. p. 264° (decomp.). [j] Not obtained completely pure; Schofield and Simpson [3] give m. p. 268° (decomp.). [k] 80% of the product isolated separated during the reaction as a nitrobenzene-insoluble titanium chloride complex which was filtered off and decomposed with boiling N-sodium hydroxide, to give a solution from which the required cinnoline was precipitated on acidification. The remainder of the product was recovered from the nitrobenzene solution in the usual way. [l] Obtained from cyclisation of (IV; R = 3-Cl, R′ = 4-Cl), after two crystallisations from acetic acid. Assigned structure based on the fact that the decarboxylated product and two derivatives, *4-acetoxy-5,6-dichloro-* and *5,6-dichloro-4-phenoxy-cinnoline* had m.p.s different from those reported for the corresponding 6,7-dichloro-isomers (see below and Table 6). [m] From crude acid chloride prepared *in situ* by treating (III; R = 3-Br, R′ = 4-Me) with thionyl chloride in benzene and subsequently evaporating the solvent *in vacuo*. [n] One crystallisation gave a single isomer the orientation of which has not been studied. [o] Needles unless otherwise stated. [p] Plates. [q] Prisms.

and extracted twice with hot 4N-sodium hydroxide (5·2 and 2·5 l.). Acidification of the combined filtrates with concentrated hydrochloric acid gave the crude acid (757 g.). A portion (400 g.) of this material was stirred with concentrated nitric acid (800 ml.) at 15° for 18 hr. The purified acid was precipitated when the solution was poured on ice. 4-Hydroxycinnoline-3-carboxylic acid (809 g.), m. p. 255—257° (decomp.), was thus obtained from the crude acid (3 × 400 g.).

4-Hydroxy-8-methoxycinnoline-3-carboxylic Acid.—Titanium tetrachloride (4·2 ml.) was added to mesoxalyl chloride *o*-methoxyphenylhydrazone (9·3 g.) dissolved in dry nitrobenzene (60 ml.). The solution was heated at 95° for 4 hr., during which it set to a black jelly. Boiling water (200 ml.) was added and the nitrobenzene was steam-distilled. The solid residue was extracted with 0·2N-sodium hydroxide (120 ml.), the extract filtered through " Hyflo Supercel," and the filtrate acidified. The purple precipitate was extracted with boiling concentrated hydrochloric acid (2 × 100 ml.), giving an insoluble black residue (4·2 g.), m. p. >360°. The combined extracts were diluted with water (800 ml.), and the precipitate (1·2 g.) was crystallised from acetic acid to give the carboxylic acid, pink needles, m. p. 274—275° (decomp.). The same yield was obtained when dry chlorobenzene was used as solvent under similar conditions.

4-Hydroxy-8-nitrocinnoline-3-carboxylic Acid.—A solution of mesoxalyl chloride *o*-nitrophenylhydrazone (67 g.) and titanium tetrachloride (32·5 ml.) in dry nitrobenzene (350 ml.) was heated at 95° for 8 hr. The solution was then poured into boiling water (4·5 l.), and the nitrobenzene removed by steam-distillation. The residual solution was filtered and cooled in ice. The yellow solid (32 g.), m. p. 180—190° (decomp.), which separated was dried and extracted with boiling ethyl acetate (400 ml.). The insoluble residue (6·9 g.) crystallised from acetic acid (300 ml.), giving the *nitro-acid* (5 g., 12%) as pale green plates, m. p. 253—254° (decomp.).

4-Hydroxy-6-nitrocinnoline-3-carboxylic Acid.—This *acid* was prepared by a method similar to that used for the 8-nitro-isomer.

5-Chloro-4-phenoxycinnoline.—5-Chloro-4-hydroxycinnoline (64 g.) was stirred with phosphorus pentachloride (84 g.) and phosphorus oxychloride (250 ml.) at 95° for 1 hr. After being cooled, the precipitate was collected and washed with successive portions of dry toluene and dry ether to give crude 4,5-dichlorocinnoline hydrochloride (71·3 g., 85%). This was added during 5 min. to an azeotropically dried suspension of potassium phenoxide [prepared from potassium hydroxide (44 g.) and phenol (300 g.)] in benzene (2 l.) at 70—80°. The solvent was evaporated *in vacuo* and the residue heated on the steam-bath for 1 hr. After being cooled, the product was extracted with chloroform (1 l.), and the extract was washed with 0·5N-sodium hydroxide (3 × 6 l.) and brine (3 × 250 ml.) and dried (Na_2SO_4). Evaporation of the solvent and crystallisation of the residue from light petroleum (b. p. 100—120°; 360 ml.) gave *5-chloro-4-phenoxycinnoline* (53·5 g., 69%) as brown prismatic needles, m. p. 115—117°; a further crystallisation raised the m. p. to 118—119° (Found: C, 65·7; H, 3·8; N, 10·8; Cl, 14·0. $C_{14}H_9ClN_2O$ requires C, 65·4; H, 3·5; N, 10·9; Cl, 13·8%). Keneford and Simpson [18] give m. p. 127—128° for 7-chloro-4-phenoxycinnoline.

4-Amino-5-chlorocinnoline.—This *base* was prepared from 5-chloro-4-phenoxycinnoline by the method of Keneford, Schofield, and Simpson [19] and obtained as fawn needles, m. p. 178—179° (Found: C, 52·7; H, 3·7; N, 23·2; Cl, 19·5. $C_8H_6ClN_3$ requires C, 53·3; H, 3·3; N, 23·4; Cl, 19·8%). Keneford *et al.*[19] give m. p. 209—210° for 4-amino-7-chlorocinnoline.

4-Acetoxy-5,6-dichlorocinnoline.—5,6-Dichloro-4-hydroxycinnoline (1·1 g.) and acetic anhydride (5·5 ml.) were heated under reflux for 1 hr. The mixture was poured on ice, and the product which separated recrystallised from light petroleum (b. p. 80—100°) to give *4-acetoxy-5,6-dichlorocinnoline* (1 g.) as colourless prisms, m. p. 178—179° (Found: C, 46·9; H, 2·4; N, 11·0; Cl, 27·1. $C_{10}H_6Cl_2N_2O_2$ requires C, 46·7; H, 2·3; N, 10·9; Cl, 27·6%). A mixed m. p. with 4-acetoxy-6,7-dichlorocinnoline,[20] m. p. 148—149°, was 125°.

5,6-Dichloro-4-phenoxycinnoline.—5,6-Dichloro-4-hydroxycinnoline (1·5 g.), phosphorus pentachloride (1·5 g.), and phosphorus oxychloride (4 ml.), were heated on a steam-bath for 1·5 hr. The 4,5,6-trichlorocinnoline hydrochloride (1·4 g.) was filtered off from the cooled mixture and washed with light petroleum (b. p. 60—80°). This material was heated with phenol (3 g.) and powdered potassium hydroxide (0·5 g.) at 95° for 1 hr. with occasional stirring.

[18] Keneford and Simpson, *J.*, 1947, 917.
[19] Keneford, Schofield, and Simpson, *J.*, 1948, 358.
[20] Keneford and Simpson, *J.*, 1947, 227.

TABLE 6. 4-*Hydroxycinnolines* (VI).

R	R′	Method	Form [x]	M. p.[a]	Yield (%)	Formula	Found (%) C	H	N	Hal	Required (%) C	H	N	Hal
H	H	[b]	Colourless [c]	236—237° [d]	82 [t]	$C_8H_6N_2O$								
8-Me	H	A	Fawn [e]	219—221 [f]	56	$C_9H_8N_2O$								
6-Me	H	A	Fawn [g]	271	64	$C_9H_8N_2O$	67·9	5·2	17·7	—	67·5	5·0	17·5	—
8-Cl	H	B	Colourless [g]	198—199 [h]	74 [i]	$C_8H_5ClN_2O$	—	—	—	—	—	—	—	—
5-Cl	H	A	Fawn [j]	330—332 [k]	70 [l]	$C_8H_5ClN_2O$	53·2	3·2	15·8	19·4	53·2	2·8	15·5	19·7
6-Cl	H	B	Fawn [c]	296 [m]	85 [i]	$C_8H_5ClN_2O$	53·5	3·3	15·6	19·8	53·2	2·8	15·5	19·7
7-Cl	8-Cl	A	Colourless [g]	261—262 [n]	95 [i]	$C_8H_4Cl_2N_2O$	—	—	13·2	33·4	—	—	13·0	33·0
6-Cl	8-Cl	A	Grey [g]	221—223	90	$C_8H_4Cl_2N_2O$	44·5	2·0	12·8	33·0	44·7	1·9	13·0	33·0
5-Cl	8-Cl	A	Colourless [g]	222—224	70	$C_8H_4Cl_2N_2O$	—	—	13·1	32·8	—	—	13·0	33·0
5-Cl	6-Cl	A	Fawn [g]	336—337 [p]	65	$C_8H_4Cl_2N_2O$	44·9	3·3	13·2	32·8	44·7	1·9	13·0	33·0
6-Br	H	A	Fawn [c]	277—278 [q]	45	$C_8H_5BrN_2O$	—	—	—	—	—	—	—	—
5(or 7)-Br	6-Me	A	Colourless [s]	288—289 [r]	45	$C_9H_7BrN_2O$	—	—	11·8	33·0	—	—	11·7	33·5
8-OMe	H	A	Colourless [t]	162—163	96	$C_9H_8N_2O_2$	61·7	4·8	15·9	—	61·4	4·5	15·9	—
6-OMe	H	[v]	Grey [w,y]	254—255 [w]	31	$C_9H_8N_2O_2$	—	—	—	—	—	—	—	—
6-NO_2	H	A	Yellow [g,z]	336 [u]	70	$C_8H_5N_3O_3$	—	—	—	—	—	—	—	—

[a] M. p. of a pure sample. [b] Decarboxylation in Dowtherm. [c] From ethanol. [d] Schofield and Simpson [9] give m. p. 233—234°; Leonard and Boyd [11] give m. p. 236°. [e] The product crystallised when hydrochloric acid was added to a solution of the cinnoline in 20% aqueous sodium hydroxide. [f] Keneford, Morley, and Simpson (*J.*, 1948, 1702) give m. p. 220—221°. [g] From acetic acid. [h] Schofield and Simpson (*J.*, 1945, 520) give m. p. 198—199°. [i] Overall yield on stages I—VI greater than 35% on a kg. scale. [j] From dimethylformamide. [k] Atkinson and Simpson (*J.*, 1947, 232) give m. p. 276—277° for 7-chloro-4-hydroxycinnoline. [l] Overall yield on stages I—VI 28% on a kg. scale. [m] From methanol. [n] Schofield and Swain [8] give m. p. 294—295°. [o] Keneford and Simpson [20] give m. p. 253—254°. [p] Mixed m. p. 299—304° with 6,7-dichloro-4-hydroxycinnoline (m. p. 340—342°) prepared by the method of Keneford and Simpson [20] who give m. p. 333—334°. For comparison of the corresponding 4-acetoxy- and 4-phenoxy-derivatives see below. [q] Schofield and Swain [8] give m. p. 286—287°. [r] Orientation of bromo-substituent R not studied. [s] From 2-ethoxyethanol. [t] From water. [u] Borsche and Herbert [10] give m. p. 338—340°. [v] Precipitated from benzophenone with ether and repeatedly extracted with water. [w] Schofield and Simpson [9] give m. p. 255—256°. [x] Needles unless otherwise stated. [y] Plates. [z] Prisms.

TABLE 7. *Miscellaneous compounds of type* (VII).

R	A	B	Active methylene compound used	Yield (%)		M. p.	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
H	CO_2Et	CN	$CN{\cdot}CH_2{\cdot}CO_2Et$	93		124—125° [a,b]	$C_{11}H_{11}N_3O_2$								
p-Cl	CO_2Et	CN	,,	96	α-form	157—158 [c]	$C_{11}H_{10}ClN_3O_2$	52·55	4·0	16·6	14·0	52·6	4·0	16·7	14·2
					β-form	124—125 [d]		52·5	4·3	—	14·35	52·6	4·0	—	14·2
p-OMe	CO_2Et	CN	,,	98	α-form	120 [c,e]									
					β-form	81—82 [f]	$C_{12}H_{13}N_3O_3$	58·0	5·3	17·0	—	58·3	5·3	17·0	—
p-NHAc	CO_2Et	CN	,,	75		210 [g]	$C_{13}H_{14}N_4O_3$	56·8	5·1	20·0	—	56·9	5·1	20·4	—
p-Me	CO_2Me	CO_2Me	$CH_2(CO_2Me)_2$	78		84—85 [h]	$C_{12}H_{14}N_2O_4$	57·6	5·8	11·5	—	57·6	5·6	11·2	—
p-Cl	CN	CN	$CH_2(CN)_2$	66		187 [i,j]	$C_9H_3ClN_4$	53·1	2·6	—	17·3	52·8	2·4	—	17·4
H	CO_2Et	NO_2	$NO_2{\cdot}CH_2{\cdot}CO_2Et$ [k]	56		60—61 [l,m]	$C_{10}H_{11}N_3O_4$	—	—	—	—	—	—	—	—
p-Cl	CO_2Et	NO_2	,,	40		118—119 [i]	$C_{10}H_{10}ClN_3O_4$	44·7	3·7	14·8	12·9	44·3	3·7	15·4	13·05
p-Cl	COMe	COMe	CH_2Ac_2	96		132—133 [i]	$C_{11}H_{11}ClN_2O_2$	55·4	4·6	11·7	—	55·3	4·6	11·7	—
p-OMe	COMe	COMe	,,	96		100—101 [i]	$C_{12}H_{14}N_2O_3$	61·5	6·1	12·2	—	61·6	6·0	12·0	—

[a] From benzene. [b] Hantzsch and Thompson [3] give m. p. 125° for the α-form. [c] Precipitated from alkaline solution by 2N-HCl. [d] Precipitated from alkaline solution by CO_2. [e] Lax (*J. prakt. Chem.*, 1901, **63**, 1) gives m. p. 116—118° for this form. [f] From aqueous ethanol; Lax (*loc. cit.*) gave m. p. 85° for this form. [g] From pyridine–water (1 : 1). [h] From methanol; Bülow and Ganghöfer [5] give m. p. 88—89°. [i] From ethanol. [j] Lythgoe, Todd, and Topham (*J.*, 1944, 315) give m. p. 188—190°. [k] As the ammonium salt. [l] From light petroleum (b. p. 40—60°). [m] Meyer and Wertheimer (*Ber.*, 1914, **47**, 2374) give m. p. 60°.

The cooled melt was mixed with an excess of 2N-sodium hydroxide, and the product extracted with chloroform; the extract was washed with alkali and then with water and dried (Na_2SO_4). Evaporation gave crude *5,6-dichloro-4-phenoxycinnoline* (1·45 g.) which crystallised from benzene–light petroleum (b. p. 80—100°) in colourless needles, m. p. 189° (Found: C, 58·0; H, 2·7; N, 9·6; Cl, 24·2. $C_{14}H_8Cl_2N_2O$ requires C, 57·8; H, 2·7; N, 9·6; Cl, 24·4%). 6,7-Dichloro-4-phenoxycinnoline is reported by Keneford and Simpson [20] to have m. p. 162—163°.

4-Hydroxycinnolines (VI).—Substituted 4-hydroxycinnoline-3-carboxylic acids were most conveniently decarboxylated by heating them in benzophenone (4 parts) at 180—210° (internal temperature) until the evolution of carbon dioxide ceased (30—60 min.[9]). The 4-hydroxycinnolines (see Table 6) were isolated in a highly pure form: (*A*) by extracting the benzophenone with ether or light petroleum (b. p. 80—100°), dissolving the residue in hot 5N-sodium hydroxide or ammonia, and reprecipitating the product with acid; or (*B*) by extracting the 4-hydroxycinnoline directly from the benzophenone into boiling N-sodium carbonate solution and reprecipitating the product with acid. The foregoing method was used to prepare 4-hydroxycinnoline [9] but on a kilogram scale higher yields were obtained when this decarboxylation was carried out in boiling Dowtherm from which the product crystallised on cooling.

Ethyl Mesoxalate 2,4-*Dinitrophenylhydrazone*.—This was prepared by heating a solution of diethyl mesoxalate (4·35 g.) and 2,4-dinitrophenylhydrazine (4·95 g.) in acetic acid (100 ml.) at 95° for 2 hr. After being cooled the mixture was poured with stirring into ice-water (800 ml.), and the bright yellow solid was filtered off and washed with water (7·4 g., 83%; m. p. 108—109°). This product (2 g.) was extracted with boiling light petroleum (b. p. 60—80°; 600 ml.), and the hot extract filtered from an unidentified by-product. The filtrate on cooling deposited the pure diester as bright yellow prisms (1·3 g., 55%), m. p. 116—117° (Found: C, 44·2; H, 3·95; N, 15·8. Calc. for $C_{13}H_{14}N_4O_8$: C, 44·1; H, 3·95; N, 15·8%). Allen [21] gave m. p. 128° (from ethanol).

Dimethyl Mesoxalate o-*Methoxyphenylhydrazone*.—This was prepared by addition of a diazonium solution, prepared in the usual way from *o*-anisidine (62·5 g.), to a stirred mixture of dimethyl malonate (66 g.), anhydrous sodium acetate (150 g.), methanol (1 l.), and water (400 ml.), at 20°. After working up as previously described for the diethyl mesoxalate phenylhydrazones and recrystallisation from methanol, the dimethyl ester was obtained as orange yellow plates (101 g., 76%). A sample recrystallised from methanol had m. p. 111—112° (Bülow and Ganghöfer [5] give m. p. 112—113°).

Other *derivatives* of type (VII) prepared similarly by coupling diazotised amines with the appropriate active methylene compound are shown in Table 7.

Methyl Hydrogen Mesoxalate p-*Tolylhydrazone*.—Dimethyl mesoxalate *p*-tolylhydrazone (50 g.) in boiling methanol (100 ml.) was treated with 2·46N-methanolic sodium hydroxide (81 ml.). After being refluxed for a short time the mixture solidified and after being cooled it was diluted with ether, and the yellow sodium salt was filtered off and washed with ether. The dry sodium salt was ground with an excess of 2N-hydrochloric acid, and the solid was filtered off, washed well with water, and recrystallised from methanol, to give the *hydrazone* 24 g., 49%), m. p. 153—154° (Found: C, 55·8; H, 5·35; N, 11·85. $C_{11}H_{12}N_2O_4$ requires C, 55·8; H, 5·1; N, 11·9%).

Methyl Glyoxylate p-*Tolylhydrazone*.—Methyl hydrogen mesoxalate *p*-tolylhydrazone (20 g.) was heated in an oil-bath at 165° (internal temperature) until evolution of carbon dioxide had ceased. The cold residue was triturated with excess of light petroleum (b. p. 40—60°), and the undissolved *α-form* of *methyl glyoxylate* p-*tolylhydrazone* (5·1 g., 31%) filtered off and washed with light petroleum. After crystallisation from methanol it had m. p. 174—175° (Found: C, 62·6; H, 6·4; N, 14·6. $C_{10}H_{12}N_2O_2$ requires C, 62·5; H, 6·25; N, 14·6%). Evaporation of the light petroleum filtrate and washings gave a syrup which when triturated with methanol at −40° gave the β-*form* (9·5 g., 58%), m. p. 21—22°. A sample recrystallised from light petroleum (b. p. 40—60°) below 0° had m. p. 21—22° (Found: C, 62·7; H, 6·2; N, 14·8%).

Ethyl Glyoxylate p-*Chlorophenylhydrazone*.—Ethyl hydrogen mesoxalate *p*-chlorophenylhydrazone (20 g.) was heated in an oil-bath to 178° (internal temperature), kept at 175—180° until no more carbon dioxide was evolved, and then cooled. Light petroleum (b. p. 40—60°) was added and the crude *ethyl glyoxylate* p-*chlorophenylhydrazone* (14·7 g., 87%) was filtered off. Crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave the pure *α-form*,

[21] Allen, *J. Amer. Chem. Soc.*, 1930, **52**, 2955.

TABLE 8. *Unsymmetrical acid chlorides* (VII; A = COCl).

TABLE 8. *Unsymmetrical acid chlorides* (VII; A = COCl).

B	R	Solvent	M. p.	Yield (%)	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
CO_2Et	*p*-Me	C_6H_6	76°	45	$C_{12}H_{12}ClN_3O_3$	54·0	4·9	10·7	13·2	53·6	4·8	10·4	13·2
CN	*p*-Cl [a]	,,	151—154	65	$C_9H_3Cl_2N_3O$	—	—	—	28·9	—	—	—	29·3
CN	*p*-OMe [b]	$CHCl_3$	138—140	68	$C_{10}H_6ClN_3O_2$	—	—	—	15·05	—	—	—	14·95
H	*p*-Cl	,,	127—128	49	$C_8H_4Cl_2N_2O$	—	—	—	32·75	—	—	—	32·8
CO_2Et	*p*-O·CH_2Ph	None [c]	105—107	85 [d]	$C_{18}H_{17}ClN_2O_4$	—	—	—	—	—	—	—	—

[a] *Anilide*, m. p. 218—219° (from ethanol) (Found: C, 60·45; H, 3·8; N, 18·6; Cl, 11·8. $C_{15}H_{11}ClN_4O$ requires C, 60·3; H, 3·7; N, 18·7; Cl, 11·9%). [b] *Anilide*, m. p. 167—169° (from ethanol) (Found: C, 65·5; H, 4·9; N, 19·0. $C_{16}H_{14}N_4O_2$ requires C, 65·3; H, 4·75; N, 19·0%). [c] Sodium salt of acid treated with thionyl chloride. [d] Crude yield; a pure sample was not obtained.

TABLE 9. *Attempted cyclisations of other compounds of type* (VII).

A	B	R	Conditions	Temperature	Result
CO_2Me	CO_2Me	*o*-OMe, *p*-Me	Thermal cyclisation in refluxing Dowtherm (250—260°) or benzophenone (297°)		Complete breakdown with evolution of MeOH or EtOH and HCN [a]
CO_2Et	CO_2Et	H, *p*-Cl, *p*-Me, *p*-NO_2, *p*-NHAc, *p*-NH·CO_2Et			
CO_2H	CO_2Et	*p*-Me	,,	,,	
CO_2Me	H	(α- and β-) *p*-Me	,,	,,	
CO_2Et	H	(α- and β-) *p*-Cl	,,	,,	
CO_2H	CO_2Et	*p*-Me, *p*-NHAc	Conc. H_2SO_4	Recovery of starting material or sulphonation at room temp.; sulphonation and/or decomp. at 60—95°	
CO_2H	CO_2H	*p*-Cl	,,	,,	
Ac	Ac	*p*-Cl, *p*-OMe	,,	,,	
CN	CO_2Et	H, *p*-NHAc	,,	Room temp.	Recovery of starting material or sulphonation [b]
CN	CN	*p*-Cl	,,	,,	Hydrolysis to *monoamide* [c]
CO_2Et	CO_2Et	*p*-Cl	Polyphosphoric acid	Recovery of starting materials at room temp. or 45—100°; decomp. at 100—165°	
CO_2H	CO_2Et	H, *p*-Cl, *p*-Me, *p*-NHAc	,,	,,	
CO_2H	CO_2H	H, *p*-Me, *o*-OMe, *p*-NO_2	,,	,,	
CN	CN	*p*-Cl	,,	,,	
Ac	Ac	*p*-Cl	,,	,,	
CO_2Et	CO_2Et	*p*-Br	Conc. H_2SO_4–Ac_2O [d]	60—95°	Monosulphonated derivative [e] of diethyl mesoxalate *p*-bromophenylhydrazone isolated as Na salt in low yield
CO_2Et	CO_2Et	*p*-Cl	BF_3–Et_2O	110—120°	BF_2 complex, m. p. 193—194°, giving ethyl hydrogen mesoxalate *p*-chlorophenylhydrazone [f] with acetic acid
CO_2H	CO_2Et	*p*-NO_2, *p*-Me, *p*-NHAc	$POCl_3$	107°	Intractable by-product and some starting material recovered
CO_2H	CO_2H	H, *p*-Me			
CO_2H	CO_2H	*p*-Me, *p*-NHAc	Anhyd. HF	0—15°	Recovery of starting material
CO_2H	CO_2H	*m*-Cl	F·SO_3H	40°	Recovery of starting material

[a] In the case of (VII; A = B = CO_2Et, R = *p*-NH·CO_2Et), there was obtained a 46% yield of p-*ethoxycarbonylaminophenyl isocyanate*, m. p. 64—65° [from light petroleum (b. p. 40—60°)] (Found: C, 58·5; H, 4·8; N, 13·6; OEt, 22·3. $C_{10}H_{10}N_2O_3$ requires C, 58·4; H, 4·85; N, 13·7; OEt, 21·85%), giving on treatment with ethanol the corresponding diurethane, 1,4-diethoxycarbonylaminobenzene, m. p. 193—194° (from ethanol) (Schiff and Ostrogovitch, *Annalen*, 1896, **293**, 371, give m. p. 196—196·5°). [b] In the case R = H, the monosulphonated derivative was isolated as its *sodium salt* (from water), no m. p. <360° (Found: C, 41·3; H, 3·1; N, 13·2; S, 10·0. $C_{11}H_{10}N_2NaO_5S$ requires C, 41·3; H, 3·3; N, 13·2; S, 10·3%) (cf. Marquardt, *J. prakt. Chem.*, 1895, **52**, 175). [c] M. p. 266° (from acetic acid) (Found: C, 48·3; H, 3·1; Cl, 15·9. $C_9H_7ClN_4O$ requires C, 48·8; H, 3·4; Cl, 16·2%). [d] Cf. Bangdiwala and Desai.[13] [e] From water (Found: Br, 18·0; N, 6·4; Na, 4·5; S, 7·1. $C_{13}H_{14}BrN_2NaO_7S$ requires Br, 17·9; N, 6·3; Na, 5·2; S, 7·2%). In acetic acid or toluene. [f] M. p. and mixed m. p. 171°.

m. p. 151—152° (Found: C, 53·0; H, 5·0. $C_{10}H_{11}ClN_2O_2$ requires C, 53·0; H, 4·85%). Crystallisation from ethanol gave the β-*form*, m. p. 68—69°, identical with the product obtained (16%) after dry distillation of the crude material obtained by coupling of *p*-chlorobenzenediazonium chloride with potassium ethyl malonate (m. p. 69—70°; mixed m. p. 68—70°) (Found: C, 53·0; H, 5·0; Cl, 15·6. $C_{10}H_{11}ClN_2O_2$ requires C, 53·0; H, 4·85; Cl, 15·7%).

Cyanoglyoxylic Acid p-*Methoxyphenylhydrazone*.—The cyanoglyoxylic esters were surprisingly resistant to mild alkaline hydrolysis, being substantially unchanged after 1 hr. at 55° with an excess of 2N-aqueous-alcoholic potassium hydroxide. With 2N-aqueous sodium hydroxide at 95°, however, the cyano-group was attacked, and then decarboxylation of the diacid occurred. The best yield of the required cyano-acid was obtained by the following procedure. Ethyl cyanoglyoxylate *p*-methoxyphenylhydrazone (26·8 g.) was dissolved in 2N-sodium hydroxide (108 ml.) and after addition of further 2N-sodium hydroxide (324 ml.) the solution was heated at 65—70° for 80 min., cooled, and kept at room temperature overnight. Cautious acidification with 2N-hydrochloric acid gave the crude acid (24·7 g.), m. p. 146—148°. Extraction of this with boiling light petroleum (b. p. 60—80°; 500 ml.) gave a product sufficiently pure for further use (22·7 g., 95%; m. p. 150—152°). In some experiments the α-form of the starting ester was recovered from the petroleum extracts (m. p. and mixed m. p. 118—119°). A sample of the *acid*, crystallised (on a small scale only) from acetic acid, had m. p. 154—155° (Found: C, 55·1; H, 4·34; N, 18·8. $C_{10}H_9N_3O_3$ requires C, 54·9; H, 4·1; N, 19·1%). Crystallisation on a large scale gave much lower yields owing to partial decarboxylation. Attempted crystallisation from aqueous ethanol resulted in complete decarboxylation to give *glyoxylonitrile* p-*methoxyphenylhydrazone* (VII; A = CN, B = H, R = *p*-OMe), m. p. 127—128° (Found: C, 61·5; H, 5·38; N, 23·7. $C_9H_9N_3O$ requires C, 61·7; H, 5·15; N, 24·0%).

Cyanoglyoxylic acid p-*chlorophenylhydrazone*, m. p. 160—161° (from ethanol) (Found: C, 48·3; H, 2·6; N, 18·9; Cl, 15·7. $C_9H_6ClN_3O_2$ requires C, 48·3; H, 2·7; N, 18·8; Cl, 15·9%), was obtained similarly in 57% yield.

Glyoxylic Acid p-*Chlorophenylhydrazone*.—This was prepared only in low yield by hydrolysis of the ethyl ester with N-aqueous-alcoholic potassium hydroxide at 60°. Crystallisation from acetic acid gave the pure acid (9%), m. p. 143—144° (decomp.) [lit.,[22] 142° (decomp.)]. The acid decomposed when kept or on attempted large-scale recrystallisation and was best stored as the stable sodium salt, prepared as follows: Ethyl glyoxylate *p*-chlorophenylhydrazone (109·3 g.) in boiling dry ethanol (242 ml.) was treated with 2·4N-ethanolic sodium hydroxide (242 ml.), and the mixture was refluxed for 20 min. After being cooled to 0°, the solid, which had separated, was filtered off and washed with ice-cold dry ethanol. Crystallisation from ethanol (1·3 l.) (charcoal) gave the *sodium salt* as pale yellow needles (40 g., 30%), m. p. 259—263° (decomp.) (Found: N, 11·35; Cl, 14·4; H_2O, 10·55. $C_8H_6ClN_2NaO_2,1{\cdot}5H_2O$ requires N, 11·35; Cl, 14·4; H_2O, 10·5%). Acidification of this sodium salt with ice-cold 2N-hydrochloric acid gave the acid, m. p. 134—135°, sufficiently pure to be used for preparation of the acid chloride.

Preparation of Unsymmetrical Acid Chlorides.—The glyoxylic, cyanoglyoxylic, and ethoxycarbonylglyoxylic acid chlorides were prepared by using thionyl chloride in an inert solvent as described above for the mesoxalyl chlorides. Some were characterised as anilides (see Table 8).

Cyclisation of Unsymmetrical Acid Chlorides.—*Cyclisation of ethoxycarbonylglyoxylyl chloride* p-*tolylhydrazone*. The acid chloride was prepared *in situ* from ethyl hydrogen mesoxalate *p*-tolylhydrazone (25 g.), and thionyl chloride (13 g.) in dry benzene (700 ml.), benzene being then removed *in vacuo* at 50°; it was dissolved in dry nitrobenzene (200 ml.), and stannic chloride (27·4 g.) added as catalyst. The mixture was then heated at 95° for 2 hr. and divided into four equal portions. To one of these was added 1·95 N-sodium hydroxide (190 ml.), and the mixture was steam-distilled to remove nitrobenzene. After being filtered hot from tin salts, the filtrate was acidified while hot with concentrated hydrochloric acid (45 ml.) to give crude 4-hydroxy-6-methylcinnoline-3-carboxylic acid [2·7 g., 54%; m. p. 240—250° (decomp.)]. Crystallisation from acetic acid gave the pure acid, m. p. and mixed m. p. 265—266°. Alternative methods of working up the remaining portions by acid or neutral steam-distillation gave lower yields.

Unsuccessful attempted cyclisations of other unsymmetrical acid chlorides (VII; A = COCl)

[22] Busch and Meussdörffer, *J. prakt. Chem.*, 1907, **75**, 121.

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at 95° gave only low-melting acid fractions (yield as stated) but no cinnoline: B = CO_2Et, R = *p*-O·CH_2Ph, 5% in 3·75 hr.; B = H, R = *p*-Cl, 18% in 6 hr.; B = CN, R = *p*-Cl, 17% in 5 hr.; B = CN, R = *p*-OMe, 2·5% in 6 hr.

Miscellaneous attempted cyclisations of mesoxalic and glyoxylic acid derivatives by other methods. A wide range of methods for cyclisation of acid derivatives, many of which have been successfully applied in the synthesis of 4-hydroxyquinolines, was applied to a variety of mesoxalic and glyoxylic acid derivatives (see Table 9) with uniform lack of success. In these experiments standard reaction conditions and methods of working-up which had been successful in other fields were used. In a few cases new derivatives formed by sulphonation or hydrolysis of the starting materials were isolated (see footnotes to Table 9).

The authors thank Dr. A. W. Nineham for the preparation of authentic 6-chloro-4-hydroxycinnoline-3-carboxylic acid, Dr. D. F. Muggleton for interpreting ultraviolet spectra, and Mr. S. Bance, B.Sc., F.R.I.C., for the microanalyses.

RESEARCH LABORATORIES, MAY & BAKER LIMITED,
DAGENHAM, ESSEX.

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553. *The Absolute Configuration of Rotenone.*

By G. BÜCHI, L. CROMBIE, P. J. GODIN, J. S. KALTENBRONN, K. S. SIDDALINGAIAH, and D. A. WHITING.

The absolute configuration of natural rotenone is determined at centres 6a and 5′ by exhaustive ozonolysis and oxidation. The 5′-centre was extracted from the rotenone degradation product (−)-dihydrotubaic acid as (+)-3-hydroxy-4-methylpentanoic acid. Synthesis and resolution gave the (−)-form of the latter, and this was degraded to (−)-2-methylpentan-3-ol, which can be related to L-glyceraldehyde by correlations in the literature. The 5′-centre of rotenone has the (*R*)-configuration. Ozonolysis of the enol acetate of dihydrorotenone, which has the same configuration as rotenone at positions 6a and 5′, gave (−)-D-glyceric acid containing the 6a-centre, whose configuration is therefore (*S*).

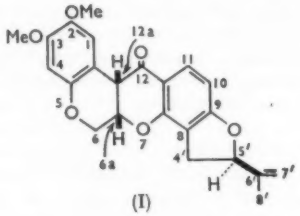
Conformation in the rotenone molecule, which has the stable form of B/C fusion, is considered. Closely related 12a-hydroxy-derivatives are shown to be more stable with a *cis*- than with a *trans*-fusion. Reduction of rotenone and compounds known to have the same B/C fusion as rotenone, [(±)-isorotenone, (−)- and (±)-dihydrodeguelin] gives crystalline 12-hydroxy-compounds which show intramolecular hydrogen bonding. This is adequately explained only when $O_{(5)}$ is the acceptor, a situation possible only with a *cis*-fusion. Other evidence supports the assignment and it is in agreement with study of the hydrogenation of rotenoid derivatives. It follows that the configuration of rotenone at 12a is (*S*), and the complete configuration is (6a*S*, 12a*S*, 5′*R*), as shown in formula (I).

STRUCTURAL investigations of the insecticidal compound rotenone, which occurs in members of the Leguminosæ, culminated in the proposal (I, without stereochemical designation).[1] The stereochemical problem could be solved by three determinations of absolute configuration, two determinations of absolute and one of relative configuration, or one determination of absolute and two of relative configuration. We have chosen the second course. First, the absolute configuration is determined at 5′, and then again at 6a since it would be difficult to relate these centres to each other. Finally, the mode of

[1] (*a*) LaForge and Haller, *J. Amer. Chem. Soc.*, 1932, **54**, 810; (*b*) Butenandt and McCartney, *Annalen*, 1932, **494**, 17; (*c*) Takei, Miyajima, and Ono, *Ber.*, 1932, **65**, 1041; (*d*) Robertson, *J.*, 1932, 1380.

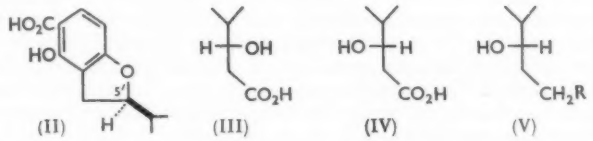
fusion of the B/C ring system is decided: this relates **6a** to **12a**. The result is shown in formula (I): rotenone has the (6a*S*,12a*S*,5′*R*) configuration.*

Rotenone is cleaved by alkali to give tubaic acid which is readily hydrogenated to dihydrotubaic acid [2] (II), retaining the rotenone configuration at position 5′. On



(I)

exhaustive ozonolysis,[3] followed by oxidation with hydrogen peroxide, dihydrotubaic acid gave (+)-3-hydroxy-4-methylpentanoic acid (III) characterised as its *p*-bromophenacyl ester. Since further degradation is required to derive a compound which has already been correlated with glyceraldehyde, supplies of the enantiomorphic acid (IV) were obtained by synthesis and resolution. A Reformatski reaction between isobutyraldehyde and benzyl bromoacetate, followed by hydrogenolysis of the benzyl grouping, gave the (±)-acid which was resolved *via* the quinine salt to give the (−)-acid (IV). The latter was reduced by lithium aluminium hydride to the (−)-diol (V; R = OH), which was converted into the monotoluene-*p*-sulphonate (V; R = $MeC_6H_4{\cdot}SO_2{\cdot}O$) and reduced



(II) (III) (IV) (V)

further with lithium aluminium hydride to (−)-2-methylpentan-3-ol (V; R = H), characterised as the (−)-3,5-dinitrobenzoate. The infrared spectra of the alcohol (V; R = H) and its 3,5-dinitrobenzoate in solution were identical with those of the racemic compounds prepared from (±)-3-hydroxy-4-methylpentanoic acid.

(−)-2-Methylpentan-3-ol has previously been correlated with L-glyceraldehyde, the isopropyl ultimately replacing the aldehyde group of the latter, and the ethyl group replacing the $\cdot CH_2OH$. The major steps in the correlation are (−)-2-methylpentan-3-ol $\xrightarrow{\text{ref. 4}}$ (+)-α-hydroxybutyric acid $\xrightarrow{\text{ref. 5}}$ (+)-β-hydroxybutyric acid $\xrightarrow{\text{ref. 6}}$ (+)-lactic acid $\xrightarrow{\text{ref. 7}}$ (+)-glyceric acid $\xrightarrow{\text{ref. 8}}$ L-(−)-glyceraldehyde: details of the intermediate transformations are contained in the references above the arrows. (+)-3-Hydroxy-4-methylpentanoic acid from (−)-dihydrotubaic acid is thus related to D-glyceraldehyde and hence rotenone has the (*R*)-configuration [9] at position 5′.

* See Büchi, Kaltenbronn, Crombie, Godin, and Whiting, *Proc. Chem. Soc.*, 1960, 274, for a preliminary communication.

[2] Takei and Koide, *Ber.*, 1929, **62**, 3030.

[3] Schmid and Ebnöther, *Helv. Chim. Acta*, 1951, **34**, 1041; Hardegger, Gempeler, and Züst, *ibid.*, 1957, **40**, 1819, and earlier papers cited there.

[4] Levene and Marker, *J. Biol. Chem.*, 1933, **101**, 413.

[5] Levene and Haller, *J. Biol. Chem.*, 1927, **74**, 343.

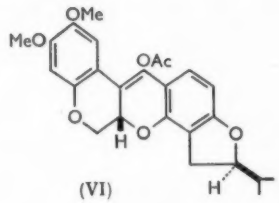
[6] Levene and Haller, *J. Biol. Chem.*, 1925, **65**, 49; 1926, **67**, 329.

[7] Freudenberg, *Ber.*, 1914, **47**, 2027.

[8] Wohl and Schellenberg, *Ber.*, 1922, **55**, 1404.

[9] (*a*) Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 81; (*b*) Feldman, *J. Org. Chem.*, 1959, **24**, 1556.

The absolute configuration at position 6a was determined as follows. Treatment of rotenone with acetic anhydride and sodium acetate yields a mixture of enol acetates epimeric at position 6a. Only one has been isolated crystalline and this has the natural configuration at $C_{(6a)}$ because acid-hydrolysis, which does not racemise the latter centre, yields only natural rotenone:[10] this has been confirmed. Also, enol acetylation of rotenone under acid conditions (isopropenyl acetate) gives the same crystalline acetate. The enol acetate was hydrogenated to acetyl 6′,7′-dihydrorotenone[11] (VI) which can also



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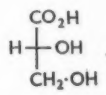

(VII)

be made direct from 6′,7′-dihydrorotenone by the isopropenyl acetate–acid technique: like acetylrotenone[10,12] it exists in dimorphic forms. Exhaustive ozonolysis of acetyl-6′,7′-dihydrorotenone gave a mixture of acids which were purified by ion-exchange chromatography. Paper chromatography[13] of the product indicated a mixture of glyceric and 3-hydroxy-4-methylpentanoic acid which was converted into the mixed *p*-bromophenacyl esters. The derivative insoluble in hot hexane was recrystallised from benzene–hexane, and had m. p. 109—111°, $[\alpha]_D^{25}$ −1·49°. Its m. p. was undepressed by varying proportions of *p*-bromophenacyl (−)-glycerate, m. p. 109—111°, $[\alpha]_D^{25}$ −1·9°, made from authentic (−)-glyceric acid[14] (VII) which has been related to D-glyceraldehyde. The hexane-soluble fraction gave the *p*-bromophenacyl ester of (+)-3-hydroxy-4-methylpentanoic acid (above). Rotenone therefore has the (*S*)-configuration at position 6a. The hydrogen atom at 6a is used as a reference point below and its orientation is designated β.

Cahn and his colleagues[10] have established that natural rotenone has the stable form of B/C fusion: they thought this might be *trans*, but reserved judgment. It was later suggested[15] that if rotenone had a *cis*-fusion a spatial relationship with DDT and methoxychlor could be developed to accommodate their common biological activity. The theory is highly speculative and no convincing chemical evidence was forthcoming. More recently, Miyano and Matsui[16] claim to have determined that rotenone has the *trans*-fusion. 6a,12a-Dehydrorotenone (VIIIa) was treated with sodium borohydride to give an amorphous alcohol (IXa) which, on Oppenauer oxidation, yielded a mixture of two diastereoisomers (" mutarotenone "),[10] one of which was natural rotenone. Such a sequence should lead to a product with the thermodynamically stable fusion and this work only confirms the earlier view.[10] Their claim to have decided from molecular models that the *trans*-B/C fusion is more stable than the *cis*- seems to us to be unacceptable.

Models for rotenone can be set up as follows. Aromatic ring D and atoms 7, 12, and 12a are coplanar or nearly so: resonance energy will be maximal if the 12-keto-group, and hence $C_{(12a)}$, is coplanar with ring D. Aromatic ring A, and atoms 5 and 12a, are coplanar, Atom 12a is common to the two approximately planar, but not coplanar, systems. Strain is taken up by deviation of atoms 6 and 6a from coplanarity with either system, *i.e.*, ring B can be a quasi-boat or quasi-chair. The two limiting conformations of the flexible

[10] Cahn, Phipers, and Boam, *J.*, 1938, 513.
[11] Smith and LaForge, *J. Amer. Chem. Soc.*, 1932, **54**, 2996.
[12] Cahn and Boam, *J. Soc. Chem. Ind.*, 1935, **54**, 42T.
[13] Palmer, *Science*, 1956, **123**, 415; *Connecticut Agr. Exp. Station Bull.*, 1955, No. 589.
[14] Anderson, *Amer. Chem. J.*, 1909, **42**, 401.
[15] Hummer and Kenaga, *Science*, 1951, **113**, 653.
[16] Miyano and Matsui, *Chem. Ber.*, 1958, **91**, 2044.

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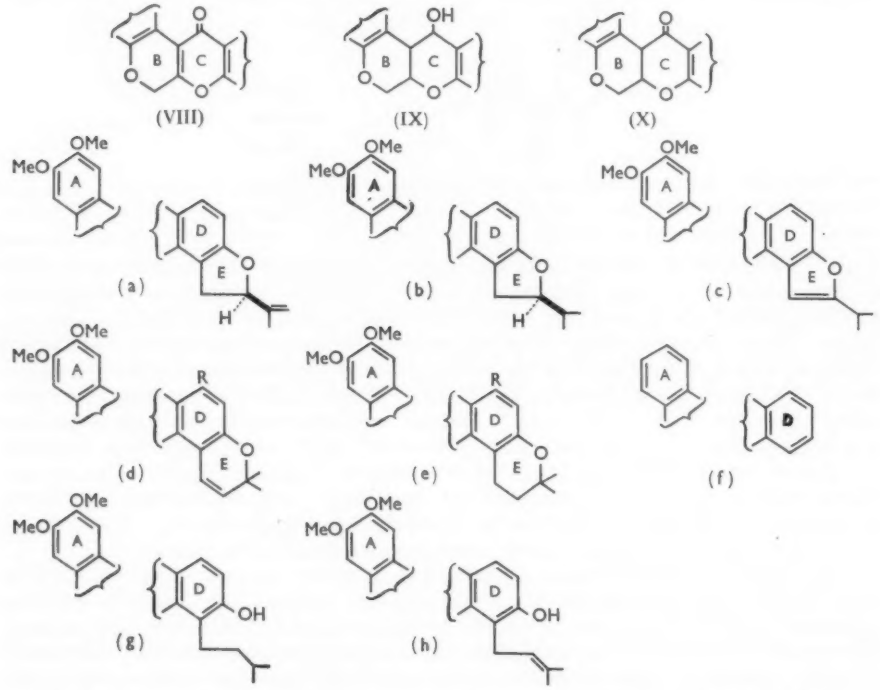
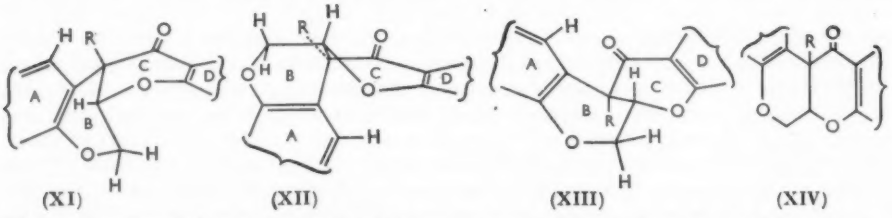
cis-fusion (XI and XII; R = H) and the one rigid *trans*-fusion (XIII; R = H) are represented in the formulæ annexed with ring B as a quasi-chair.

Natural rotenone, (—)-isorotenone [(Xc), configuratively the same at $C_{(6a)}$ and $C_{(12a)}$ as the former [10]] and other 12a-unsubstituted relatives are known only with the B/C fusion in its stable form. The difficulty attending isolation of the other fusion concerns enolisation at 12a. But in the case of the 12a-hydroxy-derivatives both fusions are known and have been



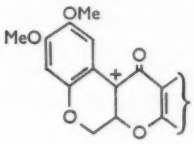
assigned by methods independent of assumptions about the configuration of rotenone itself.[17] Thus (±)-isorotenolone A is the *cis*-fused racemate (XIVc; R = OH), and (±)-isorotenolone B the corresponding *trans*-fused form. These give corresponding methyl



ethers when treated with methyl iodide and silver oxide. When the methyl ether of (±)-isorotenolone A is refluxed with methanolic sulphuric acid, except for the formation of 6a,12a-dehydro-compound (VIIIc), it is recovered unchanged. But similar treatment of the methyl ether of (±)-isorotenolone B converts it into the derivative of A (and dehydro-compound). The corresponding rotenolone methyl ethers (XIVa; R = OMe) behave

[17] Crombie and Godin, following paper; *Proc. Chem. Soc.*, 1960, 276.

analogously and the interconversion probably involves the carbonium ion (XV—XVII) which, despite its unfavourable placing α- to the ketone, is stabilised by resonance: the situation is not without precedent.[18] The partial positive charge at $C_{(12)}$ is also diminished by resonance involving the *o*- and *p*-oxygenated ring D. When acetylated by refluxing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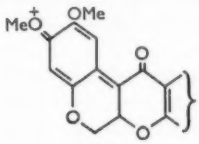
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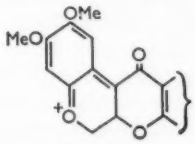
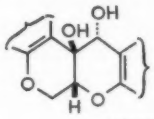

(XVII)

acetic acid–acetic anhydride containing sodium acetate, (±)-isorotenolone A and B each give 6a,12a-dehydroisorotenone and the same acetate (XIVc; R = OAc). The diol produced when the latter is reduced with lithium aluminium hydride is the same as that obtained when (±)-isorotenolone A is reduced and differs from either of the diols obtained when (±)-isorotenolone B is similarly treated. This diol is the racemate[17] (XVIIIc–XIXc), and the acetate is of the *cis*-series. It again follows that the thermodynamically stable product, produced under equilibrating conditions, has the *cis*-B/C junction. Examin-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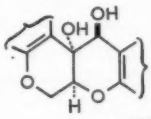
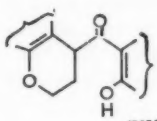
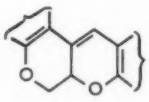
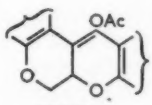

(XIX)

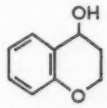

(XX)

ation of models (XI—XIII) for non-bonded interactions which might destabilise one fusion relative to the other suggests a likely cause is interaction between the 1-hydrogen and the 12-ketonic oxygen atom. In the rigid *trans*-fusion the distance between atomic centres is ~2·05 Å (ring B a quasi-chair; ~1·95 Å if a quasi-boat; measurements with Barton-type models). Interaction is relieved in the *cis*-fusion.

Direct evidence in favour of the *cis*-B/C fusion in rotenone itself was obtained as follows. Reduction of (±)-isorotenone (Xc) with potassium borohydride gave a crystalline hydroxy-compound (IXc) in more than 80% yield. The latter was also obtained by hydrogenating (±)-isorotenone in ethyl acetate over Adams platinum at 100°/60 atm. [some isorotenol (XXc) being formed], or by treating 6a,12a-dehydroisorotenone with borohydride. The hydroxy-compound (IXc) is readily dehydrated by phosphorus oxychloride in pyridine,


(XXI)


(XXII)


(XXIII)

dilute mineral acid, or chromatography on acid alumina, giving the stilbene-like compound (XXIc), and comparison of the ultraviolet absorption of the latter with that of isorotenone enol acetate (XXIIc) confirms the presence of such a chromophore.[17] Similar crystalline alcohols were also obtained from (±)- and (−)-4′,5′-dihydrodeguelin [β-dihydrorotenones, (Xe; R = H): these have the same B/C fusions as natural rotenone],[19-22] but the alcohol

[18] House and Reif, *J. Amer. Chem. Soc.*, 1955, **77**, 6525.
[19] Haller and LaForge, *J. Amer. Chem. Soc.*, 1934, **56**, 2415.
[20] Haller, *J. Amer. Chem. Soc.*, 1931, **53**, 733.
[21] Clark, *J. Amer. Chem. Soc.*, 1931, **53**, 2369.
[22] (*a*) Haller and LaForge, *J. Amer. Chem. Soc.*, 1931, **53**, 3426; (*b*) LaForge, Haller, and Smith, *Chem. Rev.*, 1933, **12**, 181.

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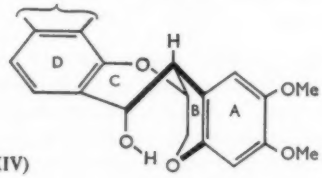
(IXa) from natural rotenone could be crystallised only as its methanol solvate. In the infrared spectrum these unsolvated alcohols showed a free (or lightly bonded) hydroxyl and a bonded hydroxyl group (the latter giving the stronger band). Figures are: (±)-(IXc), 3613, 3566 cm.$^{-1}$, Δ 47 *, Δ_s 63 *; (−)-(IXe; R = H), 3611, 3564 cm.$^{-1}$, Δ 47, Δ_s 65 (all LiF–CCl_4, c <0·005M). The solvated alcohol from rotenone has the same two bands at 3612 and 3561 cm.$^{-1}$, Δ 51, Δ_s 68, together with a third at 3641 cm.$^{-1}$ (primary hydroxyl of methanol).

Without prior assumption about the relative configurations at centres 6a, 12a, or 12, molecular models were examined to trace the acceptor seat of the hydrogen bond. Acceptors in rings C, D, or E do not offer a suitable explanation, particularly since chroman-4-ol † (XXIII) has only a single band at 3615 cm.$^{-1}$ (cf. 1-hydroxytetralin 3614 cm.$^{-1}$). There are two significant possibilities. Either the hydrogen bond is formed to aryl ring A or to $O_{(5)}$. If a *trans*-B/C fusion is postulated, bonding of the former but not the latter type is possible when the 12-hydroxyl group is β (*i.e.*, 6aβ,12aα,12β) ‡; if it is α-, neither type is feasible. With the 12-hydroxyl β, it is less well orientated towards, and more distant from, the aromatic π-electrons than in a 2-arylethanol. In comparably substituted examples of the latter a stronger bond (larger Δ and Δ_s) would be expected. Data for arylethanols are: 2-phenylethanol,[24] 3631, 3604 cm.$^{-1}$, Δ 27, Δ_s 38; 2-*m*-methoxyphenylethanol,[24] 3631, 3605 cm.$^{-1}$, Δ 26, Δ_s 37; 2-*p*-methoxyphenylethanol,[24] 3633, 3602 cm.$^{-1}$, Δ 31, Δ_s 40; 2-(3,4-dimethoxyphenyl)ethanol 3632, 3594 cm.$^{-1}$, Δ 38 Δ_s 48 (cf. 3,4-dimethoxyphenylmethanol 3612 cm.$^{-1}$). This explanation is not, therefore, supported. A *cis*-B/C fusion with a β-oriented hydroxyl (6aβ,12aβ,12β) also gives no satisfactory explanation. But when the hydroxyl is α- in this series (6aβ, 12aβ, 12α), particularly when ring B is a quasi-boat,



(XXIV)

close approach of the 12-hydroxyl to $O_{(5)}$ is possible, as in (XXIV). Conformational equilibrium will result in the presence of a free and a bonded band. Such ether bonding provides a suitable explanation for the fairly large Δ and Δ_s values and, in confirmation, 2-(3,4,6-trimethoxyphenyl)ethanol has three bands in the hydroxyl region—at 3633, 3602, and 3547 cm.$^{-1}$, Δ 31 and 86, Δ_s 40 and 95. The second band is ascribed to aryl bonding and the third to bonding to the oxygen of the 6-methoxyl group, a situation resembling that in (XXIV) but freer from geometrical restriction.§

The hydroxy-compounds of the type (IX), in the three series mentioned (a, c, and e; R = H), thus have the 12-hydroxyl group *trans* to the 12a-hydrogen atom, in agreement with the ready dehydration, and the *cis*-B/C fusion must also be present in rotenone and

* Δ = Difference between first and second hydroxyl absorption. Δ_s = Difference between second hydroxyl absorption and a standard primary (3642 cm.$^{-1}$) or secondary (3629 cm.$^{-1}$) value as appropriate.[23]

† We thank Professor O. Dann for this specimen.

‡ In the racemates, of course, 6aα, 12aβ, and 12α also; discussion is in terms of (−)-rotenone or (−)-4′,5′-dihydrodeguelin.

§ A recent report,[25] based on examination of 32 compounds having the crinane nucleus, states that the stretching frequencies for secondary hydroxyl groups bonded to the π-electrons of a double bond or an aromatic ring (substituted by methylenedioxy) occur between 3602 and 3581 cm.$^{-1}$. Hydroxyl groups bonded to adjacent ether or hydroxyl groups absorb between 3582 and 3526 cm.$^{-1}$ (weak bonds in other series give, of course, higher $\nu_{max.}$ values).

[23] Cole and Jefferies, *J.*, 1956, 4391.

[24] Schleyer, Wintner, Trifan, and Bacskai, *Tetrahedron Letters*, 1959, No. 14, 1.

[25] Fales and Wildman, Abs. Amer. Chem. Soc. 138th Meeting, Sept. 11–16, 1960, p. 19P.

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those compounds related to it. Hence natural rotenone is (6a*S*,12a*S*,5′*R*.)* † The formation of compound (XXIV) by attack of borohydride ion on the corresponding 12-ketone (XI—XII), or by catalytic hydrogenation, is as expected because approach of the reagent to the ketone or the ketone to the catalyst would involve the less hindered β-face. This is noticeable when the rotenolones and isorotenolones are reduced. The *trans*-B/C compounds (B series; XIIIa or c; R = OH) give two diols, since either face is open to attack, but it has been possible to isolate only one diol from parallel reductions among the *cis*-B/C compounds [17] (A series; XI—XIIa or c; R = OH). It is of incidental interest that *cis*-B/C forms in the rotenolones and isorotenolones and their derivatives are, in contrast to the *trans*-forms, frequently solvated. Various solvates are well known in the natural rotenoids.[27] Solvate formation may be associated with provision by the bent *cis*-skeleton, in contrast to the rigid and fairly planar *trans*-structure, of suitable lattice spaces (cf. *cis*-A/B steroids).[28] (−)-Isorotenone, with the same 6aβ,12aβ-configuration as rotenone, has a positive Cotton effect in methanol, max. 390 mμ, [α] +180°, and the curve for (+)-isorotenone is enantiomeric in detail.‡ Such information is difficult to interpret at the present time on the basis of the octant rule,[29] but a positive Cotton effect seems not inconsistent if the B/C system in rotenone is *cis*-fused.

The remainder of this paper considers the hydrogenation of unsaturated derivatives of rotenone, a process which has bearing on the stereochemistry discussed above. If 6′,7′-dihydrorotenone (Xb) has a *cis*-B/C fusion as claimed above, it should be accessible by catalytic hydrogenation, with *cis*-addition, of the 6a,12a-dehydro-compounds (VIIIa) or (VIIIb). But as proof of a *cis*-B/C fusion in rotenone such an experiment is open to objection. Thus, the addition of hydrogen might be 1,4 rather than 1,2, or the initially produced unstable fusion might stereomutate to the more stable one under the reaction conditions. There is also experimental difficulty inasmuch as the tetra-substituted pyrone double bond in the approximately planar A/B/C/D system is difficult to hydrogenate and other reactions such as 1′,5′- or 6a,7-ether cleavage, or reduction and hydrogenolysis at position 12, can occur, often critically dependent on the conditions used. In the present work, 6a,12a-dehydrorotenone (VIIIa) gave, on hydrogenation over platinum in ethyl acetate at 25°/10 atm., besides 6′,7′-dihydro-6a,12a-dehydrorotenone (VIIIb), the 1′,5′-seco-compound (VIIIg). On the other hand, hydrogenation of 6′,7′-dihydro-6a,12a-dehydrorotenone over platinum at 70°/60 atm. in the same solvent gave the 6a,7-*seco*-compound, djhydrorotenol (XXb). Nonetheless, the matter has been examined because, apart from intrinsic interest, the results must fit into a consistent and explicable pattern if our stereochemical views are accepted.

Recent writers have overlooked that the first successful 6a,12a-reduction of a rotenoid was Clark's conversion [30] of 6a,12a-dehydrotoxicarol (VIIId; R = OH) into (±)-4′,5′-dihydrotoxicarol (Xe; R = OH), identical with that made by hydrogenating (±)-toxicarol (Xd; R = OH). We have confirmed this (platinum catalyst in acetic acid at 70° and atmospheric pressure) and find that if an active catalyst is used the temperature can be lowered to 20°. Similarly, the synthetic 6a,12a-dehydro-compound [31] (VIIIf) yields

* Dr. W. D. Ollis has kindly informed us that in collaboration with Professor Djerassi it has been found that the natural rotenoids toxicarol, elliptone, pachyrrhizone, and munduserone, as well as sumatrol 11-acetate, have the same positive Cotton effect as natural rotenone.[26] It therefore seems that they also are (6a*S*,12a*S*)-compounds.

† /6/-Rotenone on the (*R*/*S*)-symbolism, /7/-rotenone on the α/β-system, according to Feldman's notation.[26]

‡ We thank Professor K. Wiesner and Dr. F. Bickelhaupt, University of New Brunswick, for these measurements.

[26] Djerassi, Ollis, and Russell, *J.*, 1961, 1448.
[27] Jones, *J. Amer. Chem. Soc.*, 1931, **53**, 2738.
[28] L. F. Fieser and M. Fieser, "Steroids," Reinhold, New York, 1959, p. 58.
[29] Moffit, Woodward, Djerassi, and Klyne, unpublished work; C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960.
[30] Clark, *J. Amer. Chem. Soc.*, 1931, **53**, 2264.
[31] LaForge, *J. Amer. Chem. Soc.*, 1933, **55**, 3040.

a ketone (Xf), the structure of which is confirmed by dehydrogenation back to (VIIIf). The ketone (Xf) is the parent of the rotenoid series and has the stable fusion since it can also be made by reducing (VIIIf) with borohydride * to give (XIXf), followed by chromic acid oxidation and is not epimerised by base. Hydrogenation of (—)-6′,7′-dihydro-6a,12a-dehydro-5′(*R*)-rotenone (VIIIb) is more complicated experimentally, since a mixture of two diastereoisomers with the same B/C fusion (6′,7′-dihydrorotenone and 6′,7′-dihydroepirotenone according to Cahn's usage,[9] or 6aβ,12aβ,5′β and 6aα,12aα,5′β) is produced. The former is readily isolated, identical with authentic material, but polarimetric results on the stereomutation of the whole product indicate that considerably more 6′,7′-dihydroepirotenone than 6′,7′-dihydrorotenone is formed. Thus, in all three hydrogenations the stable fusion is being produced from a reaction which, barring the contingencies mentioned, might be expected to give a *cis*-product. Since the 5′-isopropyl group of 6′,7′-dihydrorotenone is β-oriented (see above), the production of more *cis*-B/C material of the epi-series (6aα,12aα) than the " natural " series (6aβ,12aβ) is reasonably explained as due to hindrance by the (*R*)-5′ substituent to approach of this side to the catalyst surface. The A/B/C/D/E system of 6′,7′-dihydro-6a,12a-dehydrorotenone is approximately planar. Dann and Volz [34] have, in this connexion, recently found that hydrogenation of 6a,12a-dehydrorotenone in dimethylformamide over a palladium catalyst at 40°/250 atm. gives diastereoisomers of (IXb) which, when oxidised, produce considerably more 6′,7′-dihydroepirotenone than 6′,7′-dihydrorotenone. This agrees with our results.

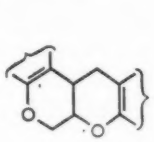
On the other hand, two recent papers [35,36] by Takahashi and his colleagues conflict with our results and, interpretatively, with each other. Thus, catalytic hydrogenation of (—)-6′,7′-dihydro-6a,12a-dehydro-5′(*R*)-rotenone, under conditions similar to those we have used, is said to lead to two diastereoisomers of dihydrorotenone belonging to the unstable or " allo " ring-junction series.[9] As the claim that rotenone is *trans* [16] is accepted, these are said to be *cis*-B/C forms. From the data given [36] we feel that these may be *cis*-forms, but mixtures of dihydrorotenone and dihydroepirotenone of the stable series and not new compounds of the " allo " series. These authors have also reported the catalytic hydrogenation of the 6a,12a-dehydro-compound (VIIIf), and their product,[35] from its m. p., is the same racemate as we obtained. Rightly, we think, they consider it a *cis*-compound, but we have shown above that it also has the stable fusion, so their views on the hydrogenation of (—)-6′,7′-dihydro-6a,12a-dehydrorotenone do not seem in accord with their own findings. Reduction of the dehydro-ketone (VIIIf) with borohydride gives an alcohol (IXf) (m. p. 180°; acetate, m. p. 163°) which is clearly different from one (m. p. 239°; acetate, m. p. 147°) isolated [37] from the mixture of products obtained when the 6a,12a-dehydro-ketone (VIIIf) is reduced over palladium at 40°/200 atm. Both, on oxidation, give the same ketone (Xf). Our alcohol of m. p. 180° is expected to be the racemate with a *cis*-B/C fusion and a *trans*-12a-H,12-OH relationship. Since the alcohol of m. p. 239° is not easily dehydrated, or easily oxidised with chromic acid, it seems reasonable that it should have a *cis*-12a-H,12-OH relationship. With a *cis*-B/C fusion the 12aα-hydrogen might be somewhat hindered to chromic acid oxidation, though because of the reaction conditions it does not necessarily follow that the parent alcohol must have the same fusion as the derived

* Presumably the unsaturated ketone is reduced 1,4 and the boron derivative decomposes under the reaction conditions to give the ketone (Xf) which is then further reduced.[16] There seems some evidence that zinc dust and alkali can cause 1,4-reduction in similar systems, since treatment of 6a,12a-dehydrorotenone can give derritol besides derrisic acid, and 6a,12a-dehydroelliptone behaves similarly.[33] This would be rational if 1,4-reduction were competing with hydrolysis of 6a,12a-dehydrorotenone, since the rotenone diastereoisomers would then undergo further degradation to derritol.[33]

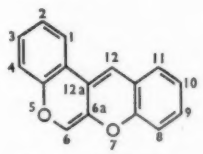
[33] Harper, *J.*, 1942, 587.
[33] Crombie, Godin, Whiting, and Siddalingaiah, *J.*, 1961, 2876.
[34] Dann and Volz, *Annalen*, 1960, **631**, 102.
[35] Fukami, Takahashi, Konishi, and Nakajima, *Bull. Agric. Chem. Soc. Japan*, 1960, **24**, 119.
[36] Takahashi, Fukami, and Nakajima, *Bull. Agric. Chem. Soc. Japan*, 1960, **24**, 123.
[37] Dann and Volz, *Annalen*, 1960, **631**, 111.

ketone. These hydrogenation experiments are thus consistent with the proposed B/C fusion.

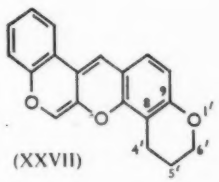
Other hydrogenation work has interest in connection with the stereochemical results obtained above. Hydrogenolysis of either (±)-4′,5′-dihydrodeguelin [(±)-β-dihydrorotenone] (Xe; R = H),* or its borohydride reduction product (IXe; R = H) gives the (±)-deoxy-compound (XXVe; R = H) which must retain the same *cis*-B/C fusion as rotenone. It has been found that catalytic hydrogenation of the (±)-12,12a-olefin (XXIe; R = H), made by dehydrating the alcohol (IXe; R = H), gives the same *cis*-B/C compound (XXVe; R = H). Experiments with (−)-4′,5′-dihydrodeguelin and with rotenone give a similar result except that in the dehydration to produce the 12,12a-olefin there is some racemisation at 6a. Thus, the hydrogenation of this olefin in the (−)-4′,5′-dihydrodeguelin series leads to *cis*-B/C compound (XXVe; R = H) which is separable into the (±)-form (above) and the (−)-form identical with the product obtained by hydrogenolysis of the (−)-ketone (Xe; R = H) or (−)-alcohol (IXe; R = H). Similarly, catalytic hydrogenolysis of rotenone, its borohydride reduction product (IXa), and rotenone enol acetate (XXIIa) all give the same compound (XXVb), $[\alpha]_D$ −148·5° to −150·5°, but dehydration of (−)-alcohol (IXa) and then hydrogenation gave (XXVb), $[\alpha]_D$ −128·2°, though identical in respect of m. p. and infrared, and ultraviolet spectra with specimens having the full optical activity. Partial racemisation during the dehydration occurs, but there may also be further racemisation during hydrogenation. Therefore, in the three examples taken, catalytic hydrogenation has occurred by attack of hydrogen on the β-face of the 12,12a-olefinic compounds (XXI) and not the α, which would give a *trans*-B/C product. Examination of molecular models indicates that in the structures (XXIe; R = H), (XXIb), and (XXIIb), $C_{(12a)}$ is perhaps less accessible to the catalyst surface from the α- than from the β-side, but the apparently high stereospecificity of attack is rather surprising. There are probably other factors also involved. If the transition state tends to resemble the final product, addition to the β-face gives a *cis*-B/C-species in which the two aromatic rings are twisted away from the catalyst and the final species would be rapidly desorbed.



(XXV)



(XXVI)



(XXVII)

Nomenclature.—Rotenoid literature abounds with trivial names for degradation products; where well established, these are used here for brevity, but confusion can arise. Thus rotenol ordinarily refers to the phenol (XXa):[38] it has been applied to a different compound,[39] and recently has been used for still a third.[16] "Ring Index" naming is cumbrous and confusing in that the essential A/B/C/D ring systems may take on different numbering, depending on the nature of ring E. A simple solution would be to give each rotenoid a trivial name and to number as in formula (I). After consultation with the

* (−)-4′,5′-Dihydrodeguelin is made by cyclising the phenolic ketone (Xh) in an acid medium. The latter ketone, which results from hydrogenation of rotenone under controlled conditions, was considered to be a product of 1,4-reduction,[19–22] but it has also been formulated [10] as a 1,2-ether cleavage product, *i.e.*, as the isopropenyl analogue of (Xh). Both structures could lead to the tertiary carbonium ion required for cyclisation. Structure (Xh) is correct, for the nuclear magnetic resonance spectrum shows two "unsaturated" methyl groups, *i.e.*, Me attached to C:C (τ 8·36 and 8·27). We thank Dr. J. W. Lown for this information

[38] Butenandt, *Annalen*, 1928, **464**, 253; cf. Haller and LaForge, *J. Amer. Chem. Soc.*, 1930, **52**, 4505; Takei, Miyajima, and Ono, *Ber.*, 1931, **64**, 1000.

[39] Takei, Koide, and Miyajima, *Ber.*, 1930, **63**, 1369.

Editor, however, we have used, where necessary, a longer but more systematic procedure. Rotenoids are named from the parent rotoxen (XXVI). The synthetic compound (VIIIf) becomes 6*H*-rotoxen-12-one † and (Xf) 6a,12a-dihydro-6*H*-rotoxen-12-one.* The compound (XXVII) is 5′,6′-dihydro-4*H*-pyrano(3′,2′-8,9)rotoxen, and natural rotenone with full configurational prefixes is 6aβ,12aβ,4′,5′-tetrahydro-2,3-dimethoxy-5′β-isopropenylfurano(3′,2′:8,9)-6*H*-rotoxen-12-one.* The prefix "seco" is useful in dealing with degradation product in which rings C or E is broken.

Experimental

Unless otherwise indicated the following apply. Ultraviolet spectra were determined for ethanol solutions: log ε in parentheses, follows $\lambda_{max.}$, and i indicates an inflexion. Infrared spectra were determined for chloroform solutions with sodium chloride optics. Molecular weights were determined ebullioscopically in benzene or chlorobenzene. In chromatographic work the letters N, A, or K together with a numeral refer to neutral, acid, and alkaline alumina of the numbered Brockmann grade. Instantaneous m. p.s determined on a Kofler hot-bar are indicated (br.). Evaporation signifies evaporation under diminished pressure, and drying infers the use of anhydrous sodium sulphate.

Rotenone.—Commercial cubé-timbo resin (2 kg.) in carbon tetrachloride (10 l.) was set aside at 0° and the crystals were filtered off and washed with carbon tetrachloride and then methanol. Dissolution in trichloroethylene, filtration, and dilution of the filtrate with methanol caused crystallisation of rotenone (654 g.). Recrystallisation from trichloroethylene and drying at 70° gave rotenone, m. p. 165—166° (or polymorph, m. p. 185—186°), $[\alpha]_D^{20}$ −228° (*c* 2·22 benzene), $\lambda_{max.}$ 217 (4·47), 236 (4·18), 244 (4·11), and 295 (4·23) mμ, $\nu_{max.}$ 1674 (C=O), 1610, 1511 (aryl), and 909 (vinyl) cm.$^{-1}$ {lit.,[40,10] m. p. 163°, 181—183° $[\alpha]_D$ −226° (in benzene)}.

Ozonolysis and Oxidation of (−)-Dihydrotubaic Acid.—Natural rotenone was degraded to tubaic acid, m. p. 128·5—130°, according to Takei and Koide's procedure [2] (lit.,[2] m. p. 129°), and this was hydrogenated in ethyl acetate over 5% palladium–barium sulphate to give (−)-dihydrotubaic acid, m. p. 167—168°, $[\alpha]_D^{25}$ −91° (in $CHCl_3$) {lit.,[2] m. p. 166°, $[\alpha]_D^{20}$ −82°}. (−)-Dihydrotubaic acid (1·05 g.) in chloroform (50 ml.) was ozonised (8 mg. of O_3/min.) at 0° for 3½ hr. The chloroform solution was poured off from a small amount of white crystalline material and evaporated to give an oil which was refluxed for 30 min. with water (25 ml.). The aqueous solution was continuously extracted with ether for 17 hr. and the extract was dried and evaporated to give a brown oil which slowly crystallised. Chromatography of the solid on silica gel from benzene and elution with benzene–ether, gave fractions which appeared from their infrared spectra to be mixtures of the expected hydroxy-keto-acid and the hydroxy-acid (III) ($\nu_{max.}$ 1742 and 1712 cm.$^{-1}$).

The brown oil (270 mg.) in 4% potassium hydroxide (10 ml.) was treated with 30% hydrogen peroxide (4 ml.) in one portion, with cooling. After 1 hr. at 20° the solution was warmed at 50° for 15 min. Water (20 ml.) was added and sulphur dioxide was passed through the solution until it was acidic to Congo Red. Extraction of the product with ether gave an oil (208 mg.) which was chromatographed on silica gel; elution with chloroform–ether (20 : 1) gave (+)-3-hydroxy-4-methylpentanoic acid (154 mg.), a liquid ($\nu_{max.}$ 1712 cm.$^{-1}$), $[\alpha]_D^{25}$ +26·4° ± 0·6° (*c* 2·1 in $CHCl_3$), characterised as the 4-*bromophenacyl ester*, m. p. 73·5—74°, $[\alpha]_D^{26}$ +13·6° ± 1° (*c* 0·74 in $CHCl_3$) (Found: C, 51·4; H, 5·35. $C_{14}H_{17}O_4Br$ requires C, 51·1; H, 5·2%).

(±)-3-*Hydroxy*-4-*methylpentanoic Acid.*—Approx. 20 ml. of a mixture of benzyl bromoacetate [41] (58·8 g.), isobutyraldehyde (19·4 g.), benzene (100 ml.), and ether (40 ml.) were added to granulated zinc (16·8 g.) with warming and stirring. When reaction started, the remainder of the mixture was added dropwise during 1 hr., sufficient heat being applied to maintain refluxing. Refluxing was continued for 1 hr. and the product was cooled and extracted with 10% sulphuric acid. The organic layer was washed with saturated sodium hydrogen carbonate solution and then water, dried ($MgSO_4$), and evaporated. Since attempted distillation caused some dehydration the crude benzyl 3-hydroxy-4-methylpentanoate (20 g.) in ethyl acetate

* This use of the suffix "one" accords with *Chemical Abstracts* practice. An alternative name for (VIIIf) is 6,12-dihydro-12-oxorotoxen; and similarly for the analogous ketones, rotenone itself having a hexahydro-prefix (not tetrahydro).

[40] Cahn, *J.*, 1934, 1129.
[41] Clarke, *J.*, 1910, 416.

(125 ml.) was hydrogenolysed over 7% palladium–strontium carbonate. The calculated amount of hydrogen was consumed in 7½ hr. and the solution was filtered through "Celite" and evaporated. The product was chromatographed on silica gel to give (±)-3-hydroxy-4-methylpentanoic acid, characterised as the (±)-4-*bromophenacyl ester*, m. p. 83·5—84° (Found: C, 51·5; H, 5·5%). The infrared spectra of this (±)-acid and its (±)-ester were identical (solutions) with those of the corresponding (+)-compounds (above).

Optical Resolution of (±)-3-*Hydroxy*-4-*methylpentanoic Acid*.—(±)-Acid (5·44 g.) in ethyl acetate (50 ml.) was added to a warm solution of quinine in ethyl acetate (200 ml.). Concentration gave a quinine salt (8·0 g.), m. p. 147·5—151·5°, $[\alpha]_D$ −143·5° ± 0·5° (in EtOH). Recrystallisation from ethyl acetate gave quinine salt (5·7 g.), m. p. 151·5—153°, $[\alpha]_D^{25}$ −145° ± 2° (*c* 1·03 in EtOH). The acid (2·9 g.), $[\alpha]_D^{28}$ −24·7° ± 0·6° (*c* 0·98 in $CHCl_3$), was isolated from this salt by treatment with 10% sulphuric acid and extraction with ether. Its infrared spectrum was identical with that of the specimen of enantiomeric (+)-acid (above). The 4-*bromophenacyl ester* had m. p. 74—75°, $[\alpha]_D^{25}$ −14·4° (*c* 2 in $CHCl_3$), and the same infrared spectrum as the (+)-ester (Found: C, 51·4; H, 5·4%).

(±)- *and* (−)-4-*Methylpentane*-1,3-*diol*.—(±)-3-Hydroxy-4-methylpentanoic acid (1·92 g.) was added dropwise to lithium aluminium hydride (0·76 g.) in ether (25 ml.), and the mixture was refluxed for 2 hr. Water (5 ml.) was added and the ethereal solution was decanted. The residue was thoroughly extracted with ether, and the combined ethereal solutions were dried and evaporated. Distillation at 10 mm. (bath 130°) gave (±)-4-methylpentane-1,3-diol (1·26 g.), characterised as the *di*-α-*naphthylurethane*, m. p. 136—137° (Found: C, 73·6; H, 6·15. $C_{28}H_{28}O_4N_2$ requires C, 73·65; H, 6·2%).

The (−)-acid (2·9 g.), similarly reduced, gave (−)-4-methylpentane-1,3-diol (2·1 g. crude) which when distilled at 13 mm. (bath 130—135°) had n_D^{25} 1·4482 and $[\alpha]_D^{27}$ −6·9° ± 0·2° (*c* 2·84 in $CHCl_3$). Its infrared spectrum was the same as that of the (±)-diol. The *di*-α-*naphthylurethane* of the (−)-diol had m. p. 134·5—136·5° (Found: C, 73·95; H, 6·4%).

(±)- *and* (−)-4-*Methyl*-1-*toluene*-p-*sulphonyloxypentan*-3-*ol*.—Toluene-*p*-sulphonyl chloride (2·03 g.) was added to (±)-4-methylpentane-1,3-diol (1·26 g.) in dry pyridine (15 ml.) with cooling. The mixture was kept at 20° for 11 hr. and then poured into ether (100 ml.) and extracted with 5% hydrochloric acid, 2% aqueous sodium carbonate, and water. The ethereal solution was dried and evaporated to give the crude (±)-toluene-*p*-sulphonate (1·47 g.) having the characteristic bands (1176 and 915 $cm.^{-1}$) of such a derivative. Attempted distillation or chromatography on alumina (N1) caused decomposition.

(−)-4-Methylpentane-1,3-diol (1·39 g.) similarly gave a crude (−)-toluene-*p*-sulphonate (1·8 g.).

(±)- *and* (−)-2-*Methylpentan*-3-*ol*.—The crude (±)-toluene-*p*-sulphonate (1·47 g.) was refluxed with lithium aluminium hydride (228 mg.) in ether (10 ml.) for 4 hr. Water (5 ml.) was added, the ether layer decanted, the residue extracted with ether, and the ethereal solution dried and evaporated. Distillation of the residue at atmospheric pressure gave (±)-2-methylpentan-3-ol (258 mg.) (bath 135—140°), n_D^{25} 1·4173 (lit.,[42] n_D^{20} 1·4175), characterised as the 3,5-*dinitrobenzoate*, m. p. 81—82° (Found: C, 52·95; H, 5·6. $C_{13}H_{16}O_6N_2$ requires C, 52·7; H, 5·45%).

Similarly the crude (−)-toluene-*p*-sulphonate (1·8 g.) gave (−)-2-methylpentan-3-ol (411 mg.), distilling at atmospheric pressure from a bath at 135—145° and having n_D^{25} 1·4184, $[\alpha]_D^{27}$ −8·5° ± 0·25° (*c* 3·31 in EtOH) {lit., $[\alpha]_D$ −9·8° (homogeneous) [4] and for the enantiomorph $[\alpha]_D$ +16·4° (*c* 1·06 in EtOH) [43]}. The 3,5-*dinitrobenzoate* had m. p. 89—92°, $[\alpha]_D^{26}$ +4·9° ± 0·6° (*c* 1·1 in $CHCl_3$) (Found: C, 52·25; H, 5·45%). The infrared spectra of the two (±)-compounds were the same as those of the two (−)-compounds.

Rotenone Enol-acetate (*Acetylrotenone*).—(*a*) Rotenone (60 g.), anhydrous sodium acetate (30 g.), and acetic anhydride (950 ml.) were refluxed for 1 hr. and the mixture was cooled and poured into water (1·6 l.) and stirred for 1 hr. The precipitated sticky solid was washed with water and crystallised from ethanol, to give rotenone enol-acetate, m. p. 160—163° (23 g.), raised by re-crystallisation to m. p. 162—164° (20·8 g.). A similar preparation gave the dimorph, m. p. 136—137° (Found: C, 68·65; H, 5·75. Calc. for $C_{25}H_{24}O_7$: C, 68·8; H, 5·55%), $[\alpha]_D^{22}$ −156° (*c* 2·05 in C_6H_6), $\lambda_{max.}$ 220 (4·40), 255 (4·15), 315 (4·04), 354 (4·54) and 372 (4·46) mμ,

[42] Pukirev, *Trans. Inst. Pure Chem. Reagents* (*U.S.S.R.*), 1939, No. 16, 73; *Chem. Abs.*, 1943, **37**, 4686.

[43] Pickard and Kenyon, *J.*, 1913, **103**, 1923.

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inflexions at 246, 263, 302 mμ, $\nu_{max.}$ 1761 (Ac), 1619 and 1502 (aryl) cm.$^{-1}$. Cahn, Phipers, and Boam [10] give m. p. 137° and 159—160°, $[\alpha]_D$ −172·5° (in C_6H_6), $\lambda_{max.}$ 250 (4·24), 354 (4·47), and 373 (4·44) mμ.

(*b*) Rotenone (1 g.), isopropenyl acetate (6 g.) and concentrated sulphuric acid (1 drop) were refluxed together for 15 min. Acetone was then gradually distilled off and finally isopropenyl acetate was removed *in vacuo*. The residue was crystallised from ethanol (charcoal), to give colourless acetylrotenone, m. p. 164—165° (Found: C, 69·0; H, 5·75%), $[\alpha]_D^{22}$ −155·5° (*c* 2 in C_6H_6), $\lambda_{max.}$ 255 (4·16), 355 (4·63), and 370 (4·44) mμ. When an ethanolic solution of the form of m. p. 136—137° was seeded with the form of m. p. 164—165° it crystallised in the higher-melting form: the infrared solution spectra of the two forms were identical.

Dihydrorotenone Enol-acetate.—(*a*) The enol-acetate of rotenone (20·6 g.) was hydrogenated in acetone (300 ml.) over 5% palladium–barium sulphate (2 g.). Filtration, working up, and crystallisation from ethanol gave dihydrorotenone enol-acetate (16·8 g.), m. p. 208·5—210·5°, $[\alpha]_D^{26}$ −161° (*c* 1·4 in C_6H_6) (lit.,[11] m. p. 209—211°).

(*b*) (−)-Dihydrorotenone (1 g.), isopropenyl acetate (6 g.), and concentrated sulphuric acid (3 drops) were boiled together for 2 hr. Working up gave the enol acetate (0·64 g.), colourless needles, in a second form, m. p. 174—175°, $[\alpha]_D^{20}$ −164° (*c* 1·4 in C_6H_6), having the same solution infrared spectrum as the higher-melting form.

Ozonolysis of Dihydrorotenone Enol-acetate.—The acetate (5 g.) in methanol–chloroform (1 : 1; 100 ml.) was ozonised at 0° for 12 hr. (50% excess). The solvent was evaporated and the oily residue refluxed for 30 min. with water (50 ml.). Evaporation of the water at 50° left a brown residue which was dissolved in methanol–chloroform (1 : 1) and again ozonised (1 hr.). Working up as before left a brown solid (4·6 g.) which was chromatographed on ion-exchange resin (Dowex 1X10; acetate form; 100—200 mesh) in a column (1·7 × 14·5 cm.) with N-acetic acid as eluant. Fractions of 25 ml. were collected and examined by paper chromatography to decide in which fractions glyceric acid was present. [The system of Palmer [13] was used: the solvent system was ethyl ether–88% formic acid–water (5 : 2 : 1), and the spray reagent a 0·04% ethanolic solution of Bromophenol Blue.] As a contaminant with high R_F value (0·96—1·00) was present, ion-exchange chromatography was repeated. Evaporation of the appropriate fractions at 50° gave a mixture (160 mg.) of glyceric and 3-hydroxy-4-methylpentanoic acid. The mixture was converted into the 4-bromophenacyl esters and crystallised from ethanol. After drying, the crystals were extracted three times with boiling hexane, and the insoluble portion was crystallised from benzene–hexane; a further recrystallisation gave the (−)-*4-bromophenacyl glycerate* (35·2 mg.), m. p. 109—111°, $[\alpha]_D^{25}$ −1·49° ± 0·2° (*c* 4·36 in acetone). The m. p. was not depressed by the authentic specimen below and the infrared spectra were identical (Found: C, 43·2; H, 3·5. $C_{11}H_{11}BrO_5$ requires C, 43·6; H, 3·65%). Chromatography of the hexane-soluble portion on alumina (N4) gave the (+)-4-bromophenacyl ester, m. p. 73—73·5°, $[\alpha]_D^{25}$ +12·2° ± 0·2° (*c* 2·31 in $CHCl_3$), of (−)-3-hydroxy-4-methylpentanoic acid. The infrared spectrum was identical with that of the specimen described above.

Optical Resolution of (±)*-Glyceric Acid.*—Glyceric acid was resolved according to Anderson's procedure [14] and gave a calcium salt, $[\alpha]_D^{24}$ +14·4° (*c* 2·12 in H_2O), {lit., $[\alpha]_D^{20}$ +14·0° (in H_2O)}. The 4-bromophenacyl ester had m. p. 109—111°, $[\alpha]_D^{25}$ −1·9° ± 0·2° (*c* 5·62 in acetone). (±)-*4-bromophenacyl glycerate* had m. p. 120—122° (Found: C, 43·2; H, 3·55%).

Treatment of (±)*-Isorotenolone A and B Methyl Ethers with Methanolic Acid.*—(±)-Isorotenolone B methyl ether [17] (200 mg.) was refluxed with concentrated hydrochloric acid (0·75 ml.) in methanol (17 ml.) for 15 min. After cooling, 6a,12a-dehydroisorotenone (71 mg.), m. p. and mixed m. p. 194—195° (decomp.), was filtered off. Evaporation gave more dehydroisorotenone (18 mg.), and then isorotenolone A methyl ether (56 mg.) as needles, m. p. and mixed m. p. 152—153° (and infrared mull comparison) after crystallisation from methanol.

(±)-Isorotenolone A methyl ether [17] (100 mg.) under identical conditions gave 6a,12a-dehydroisorotenone (31 mg.) and recovered methyl ether (48 mg.), m. p. and mixed m. p. 152°.

Acetylation of (±)*-Isorotenolone A and B.*—(±)-Isorotenolone A (400 mg.) was refluxed for 15 min. with acetic anhydride (2·5 ml.), glacial acetic acid (1 drop), and anhydrous sodium acetate (2·5 g.). Methanol was added and the mixture poured into water. The precipitate was filtered off, boiled with methanol, and freed from 6a,12a-dehydroisorotenone (160 mg.; m. p. and mixed [33] m. p. 192°) by filtration. Concentration of the filtrate gave (±)*-isorotenolone A acetate* (62 mg.), m. p. 165° (Found: C, 66·6; H, 5·3. $C_{25}H_{24}O_8$ requires C, 66·35; H, 5·35%).

(±)-Isorotenolone B (250 mg.) similarly gave 6a,12a-dehydroisorotenone (120 mg.) and

(±)-isorotenolone A acetate (32 mg.), m. p. and mixed m. p. 165°: the infrared solution spectrum was identical with that of the specimen described above, $\nu_{max.}$ 1742 (OAc), 1689 (C=O), 1618, 1595, and 1504 (aryl) cm.$^{-1}$.

(±)-Isorotenolone A acetate (50 mg.) was refluxed with acetic anhydride (0·5 ml.), glacial acetic acid (1 drop), and sodium acetate (50 mg.) for 30 min. After cooling, methanol was added: when this mixture was kept at 0°, 6a,12a-dehydroisorotenone (40 mg.), m. p. and mixed m. p. 195—196° (decomp.), separated.

Reduction of (±)-*Isorotenolone A Acetate with Lithium Aluminium Hydride.*—The acetyl compound (1 g.) in dry tetrahydrofuran was added slowly to lithium aluminium hydride (1 g.) in tetrahydrofuran (35 ml.), and the whole was stirred under nitrogen for 5 hr. Ethyl acetate and then ammonium chloride solution were added. The mixture was filtered through kieselguhr, and the filtrate was extracted with chloroform. The extract was dried and evaporated, and the residue (m. p. 208°) was chromatographed from chloroform–benzene (1 : 1) on alumina (N4) and then crystallised from chloroform–light petroleum (b. p. 60—80°), to give the (±)-*iso*-A diol [17] (XVIII—XIXc) (570 mg.), m. p. and mixed m. p. 216° (and infrared comparison). In an identical experiment, except that reflux conditions were used, the yield was 848 mg.

Reduction of (±)-*Isorotenone with Potassium Borohydride.*—(−)-Isorotenone, prepared [41] from (−)-rotenone by the sulphuric–acetic acid method, had m. p. 176° or 185°, $[\alpha]_D^{23\cdot5}$ −80° (*c* 2 in C_6H_6), $\lambda_{max.}$ 243 (4·69), 248 (4·64), 261 (4·18), 279 (4·05), and 330 (3·65) mμ, $\nu_{max.}$ 1680 (C=O), 1617, 1597, 1513 (aryl bands) cm.$^{-1}$ [lit., m. p. 176° or 184° (two forms)]; in chloroform it is dextrorotatory, $[\alpha]_D^{23}$ +8° (*c* 2).[45] Treatment with potassium carbonate in acetone [10] gave (±)-isorotenone, m. p. 172°, $[\alpha]_D$ 0°: the infrared (solution) and ultraviolet spectra were identical with those above (lit.,[19] m. p. 170—171°). (±)-Isorotenone (5 g.) in tetrahydrofuran (40 ml.) and water (20 ml.) was treated with potassium borohydride at 0° for 7 days. The mixture was refluxed for 3 hr. and then heated with 10% potassium hydrogen carbonate solution (30 ml.) overnight. The product was poured on ice and the 12α-*hydroxy-compound* (IXc) (4·12 g.) was filtered off: from chloroform–methanol it formed needles, m. p. 193° (Found: C, 69·55; H, 6·35. $C_{23}H_{24}O_6$ requires C, 69·7; H, 6·1%), $\lambda_{max.}$ 251 (4·38), 258 (4·40), 280i (4·03), 290 (4·11) and 297i (3·95) mμ, $\nu_{max.}$ 1621, 1600, 1587, and 1499 cm.$^{-1}$ (aryl).

Reduction of 6a,12a-*Dehydroisorotenone with Sodium Borohydride.*—The ketone (1 g.) in tetrahydrofuran at 50° was treated with sodium borohydride (0·4 g.) in 90% aqueous ethanol (10 ml.) and kept at 50° for 1 hr. and at 20° for 4 hr. The solution was washed with brine, dried, and evaporated, to give solid (0·9 g.) which, crystallised from methanol, gave the 12-hydroxy-compound (IXc), m. p. and mixed m. p. 192—194°. Chromatography from benzene–chloroform (1 : 1) on alumina (K1) gave unchanged material, but on alumina (A1) a yellow band appeared which on elution gave the 12,12a-dehydro-compound (XXIc), m. p. and mixed m. p. 179°.

High-pressure Hydrogenation of (±)-*Isorotenone.*—Isorotenone (3 g.) in ethyl acetate (50 ml.) was hydrogenated at 100°/60 atm. over Adams platinum catalyst for 7 days. The mixture was filtered, the filtrate evaporated, and the residue chromatographed from benzene on alumina (N1), to give isorotenol (XXc) (0·33 g.), m. p. and mixed m. p. 131—132° (Found: C, 69·9; H, 6·35. Calc. for $C_{23}H_{24}O_6$: C, 69·7; H, 6·1%). Continued elution gave the 12α-hydroxy-compound (IXc) (1·5 g.), m. p. 195° (from ethanol). Identity with the above specimen was established by mixed m. p. and infrared comparison.

Pressure Hydrogenation of 6a,12a-*Dehydrorotenone.*—6a,12a-Dehydrorotenone (9·5 g.) in ethyl acetate (200 ml.) was hydrogenated over Adams catalyst (2 g.) at 25°/10 atm. for 36 hr. The mixture was warmed and filtered and the filtrate was concentrated. 6a,12a-Dehydro-6′,7′-dihydrorotenone (3·5 g.), m. p. and mixed m. p. 226—227°, separated and was filtered off. The filtrate was evaporated and the residue was dissolved in chloroform (50 ml.) and extracted with 2% aqueous potassium hydroxide. The alkaline extracts were acidified with 4N-hydrochloric acid and extracted with chloroform. Evaporation of the extract and crystallisation from ethanol gave the 1′,5′-*seco*-compound (VIIIg), m. p. 218° (decomp.), $\lambda_{max.}$ (in acid ethanol) 241 (4·40), 276 (4·39), and 304 (4·26) mμ, $\lambda_{max.}$ (in alkaline ethanol) 204i (4·42), 270 (4·46), 282i (4·42), and 316 (4·36) mμ, $\nu_{max.}$ 3236 (intermolecularly bonded OH), 1631 (unsatd. ketone), 1603 and 1499 (aryl) cm.$^{-1}$ [lit.,[46] for (VIIIg) (" dehydrodihydrorotenonic acid "), m. p. 221°].

[41] Wright, *J. Amer. Chem. Soc.*, 1928, **50**, 3358.
[45] Butenandt and Hildebrandt, *Annalen*, 1930, **477**, 245.
[46] LaForge and Smith, *J. Amer. Chem. Soc.*, 1930, **52**, 3603.

Pressure Hydrogenation of 6a,12a-*Dehydro*-6′,7′-*dihydrorotenone*.—The ketone (2 g.) was hydrogenated over Adams catalyst (500 mg.) in ethyl acetate (25 ml.) at 70°/60 atm. for 7 days. The catalyst was filtered off, the filtrate evaporated, and the residue crystallised from ethanol, to give 6′,7′-dihydrorotenol (1·53 g.), needles, m. p. 133° (lit.,[47] 131°) (Found: C, 69·2; H, 6·55. Calc. for $C_{23}H_{26}O_6$: C, 69·35; H, 6·6%), $\nu_{max.}$ 1636 (chelated ketone), 1616, 1499, and 1484 (aryl) cm.$^{-1}$; there was a broad band beneath the C–H stretching vibrations due to the chelated hydroxyl.

Hydrogenation of 6a,12a-*Dehydro*-α-*toxicarol*.—6a,12a-Dehydro-α-toxicarol was prepared according to Cahn *et al.*[10] (who give m. p. 226—227°) and had m. p. 230—231° (Found: C, 67·1; H, 5·0; O, 27·15. Calc. for $C_{23}H_{20}O_7$: C, 67·65; H, 4·95; O, 27·4%), $\nu_{max.}$ 1654 (chelated ketone), 1613, 1578, and 1513 (aryl) cm.$^{-1}$ (the chelated hydroxyl forms a broad band at the base of the C–H vibrations), $\lambda_{max.}$ 237 (4·43), 270 (4·61), 280 (4·61), and 332 (4·17) mμ. The dehydro-compound (1 g.) was hydrogenated in glacial acetic acid over Adams platinum at 75° until 125 ml. of hydrogen (N.T.P.) had been absorbed. The catalyst was filtered off and the product was chromatographed from chloroform on alumina (N). Crystallisation gave (±)-4′,5′-dihydro-α-toxicarol, m. p. 206°, mixed m. p. 208°, $\lambda_{max.}$ 302 (4·36) mμ, $\nu_{max.}$ 1638 (chelated ketone), 1617, 1586, and 1506 (aryl) cm.$^{-1}$. The infrared spectrum was superimposable on that of the (±)-specimen below.

(±)-α-Toxicarol was catalytically hydrogenated to give (±)-4′,5′-dihydro-α-toxicarol, m. p. 209—210° (Found: C, 66·55; H, 6·0; O, 27·5. Calc. for $C_{23}H_{24}O_7$: C, 67·0; H, 5·85; O, 27·15%) (lit.,[30] m. p. 205°, clear at 209°), $\lambda_{max.}$ 300 (4·39) and 344 (3·68) mμ. (−)-4′,5′-Dihydro-α-toxicarol, made similarly, had m. p. 184—185° (Found: C, 67·0; H, 6·15%), $[\alpha]_D^{20}$ −36·6° (*c* 2 in C_6H_6) [lit.,[10] m. p. 178—180°, $[\alpha]_D$ −57° (in C_6H_6)], $\nu_{max.}$ 1639 (chelated ketone) cm.$^{-1}$, $\lambda_{max.}$ 298 (4·40) mμ; its infrared spectrum (solution) was identical with that of the (±)-form.

Reduction of 6H-*Rotoxen*-12-*one with Borohydride*.—The ketone (VIIIf) was made by La Forge's method,[31] except that dropwise addition of ethyl bromoacetate in the final stage considerably raised the yield (42%); it had m. p. 134—135° (lit.,[31] m. p. 135°) (Found: C, 76·85; H, 4·3. Calc. for $C_{16}H_{10}O_3$: C, 76·8; H, 4·05%), $\lambda_{max.}$ 217 (4·45) and 265 (4·38) mμ, and a flat inflexion between 288 and 305 mμ, $\nu_{max.}$ 1639 (unsatd. ketone), 1626, 1609, 1563, and 1494 (aromatic bands) cm.$^{-1}$. [A specimen of rotoxen-6,12-dione, made by use of ethoxalyl chloride in place of bromoacetic acid,[31] had m. p. 242—243° (lit.,[31] 240°) (Found: C, 72·85; H, 3·3. Calc. for $C_{16}H_8O_4$: C, 72·75; H, 3·05%), $\lambda_{max.}$ 234 (4·04), 250 (4·14), 265 (4·28), 279 (4·25), and 353 (3·94) mμ, $\nu_{max.}$ 1743 (lactone), 1658 (C=O), 1621, 1586, 1562, and 1494 (aromatic) cm.$^{-1}$.]

The ketone (VIIIf) (1 g.) in tetrahydrofuran (50 ml.) was warmed to 60° and potassium borohydride (0·4 g.) in 50% aqueous ethanol (10 ml.) was added. The solution was kept at 60—65° for 90 min. and then washed with saturated sodium chloride solution, dried, evaporated, and crystallised, to give the *hydroxy-compound* (IXf), m. p. 179—180°, unchanged by chromatography on alumina (K) (Found: C, 75·7; H, 5·75. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·55%), $\lambda_{max.}$ 275 (3·74) mμ, $\nu_{max.}$ (mull) 3247 (OH) cm.$^{-1}$. The *acetyl derivative* [from the chromanol (IXf) with acetic anhydride and pyridine] had m. p. 163° (Found: C, 73·2; H, 5·35. $C_{18}H_{16}O_4$ requires C, 72·95; H, 5·45%), $\lambda_{max.}$ 277 (3·74) mμ, $\nu_{max.}$ (mull) 1733 (acetate) cm.$^{-1}$. For the stereoisomer Dann and Volz report [37] m. p. 238—239° (acetyl derivative m. p. 147—147·5°).

6a,12a-*Dihydro*-6H-*rotoxen*-12-*one by Oxidation of the Hydroxy-compound* (IXf).—The hydroxy-compound (IXf), m. p. 179—180° (200 mg.), in acetone (5 ml.) was treated with chromium trioxide and kept overnight. The whole was filtered and the filtrate was diluted with water and extracted with ether, to give a solid (150 mg.) which, when crystallised from methanol, gave the ketone (Xf), m. p. 163° (Found: C, 76·5; H, 4·8. Calc. for $C_{16}H_{12}O_3$: C, 76·2; H, 4·8%), $\lambda_{max.}$ 255 (3·96) and 322 (3·47) mμ, $\nu_{max.}$ (mull) 1695 cm.$^{-1}$. The m. p. of the specimen was not depressed on admixture with Dann and Volz's ketone,[37] m. p. 165—166·5°, kindly supplied by Professor O. Dann. Fukami *et al.*[35] give m. p. 162—163° but record $\lambda_{max.}$ 225 (3·95) and 320 (3·48) mμ. The ketone (25 mg.) was unaltered when refluxed for 90 min. with potassium carbonate (10 mg.) in acetone (3 ml.). The ketone (50 mg.) and sodium acetate (150 mg.) were dissolved in ethanol (5 ml.), iodine (100 mg.) in ethanol (5 ml.) was added, and the whole was refluxed for 30 min., and then refluxed for 30 min. more with 20% ethanolic sulphuric acid (5 ml.); working up in the usual way gave the 6a,12a-dehydro-ketone (VIIIf), m. p. and mixed m. p. 133°.

6a,12a-*Dihydro*-6H-*rotoxen*-12-*one by Hydrogenation of* 6H-*Rotoxen*-12-*one*.—The ketone (VIIIf) (400 mg.) was hydrogenated over Adams catalyst (60 mg.) in acetic acid (80 ml.) at 20°

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until 1·5 mol. of hydrogen had been absorbed. The catalyst was filtered off, the filtrate diluted with much water, and the precipitate collected with ether. The ethereal solution was washed with chalk suspension, dried, and evaporated, and the residue was crystallised from aqueous ethanol to give the ketone (Xf) (m. p. 130—140°, 250 mg., crude), m. p. and mixed m. p. 163° (50 mg.) after further crystallisation from methanol. The infrared spectrum (mull) was identical with that of the specimen described above. The spectrum of the material of m. p. 130—140° showed it to be the ketone contaminated with the hydroxy-compound (IXf).

Reduction of Rotenone with Lithium Aluminium Hydride.—Rotenone (6·0 g.) in dry tetrahydrofuran (50 ml.) was treated under nitrogen with a slurry of lithium aluminium hydride (1·8 g.) in dry tetrahydrofuran. The mixture was heated under reflux for 15 min., then cooled, and water was added. The product was just acidified and extracted with chloroform. Working up in the usual way gave a foam which gave no blue Durham test, $[\alpha]_D^{20}$ −208° (*c* 2 in C_6H_6), $\nu_{max.}$ 3541 (OH), 1653 vw (C=C), 1619 and 1511 (aryl) cm.$^{-1}$, $\lambda_{max.}$ 220 (4·35) and 286 (3·79) mμ. When kept under methanol for a long period the *hydroxy-compound* (IXa) formed cubic solvated crystals, m. p. 94° with frothing (Found: C, 67·3; H, 6·55. $C_{23}H_{24}O_6,CH_3{\cdot}OH$ requires C, 67·3; H, 6·6%). Except for methanol absorption the infrared solution spectrum was identical with that of the glass above. When the crystals were heated *in vacuo* for 8 hr. at 65° the methanol absorption disappeared, but the glass obtained on cooling crystallised again only from methanol and required seeding. When the hydroxy-compound was shaken with acid alumina in chloroform, dehydration could be observed by following the decline of the infrared hydroxylic absorption.

α-Tetralol and Chroman-4-ol.—α-Tetralol was made by treating α-tetralone (5 g.) in water (5 ml.) and tetrahydrofuran (25 ml.) with potassium borohydride (2·5 g.) at 0° for some days. The mixture was refluxed for 1 hr., then refluxed for 3 hr. with 10% potassium carbonate solution and poured on ice. Isolation and working up gave α-tetralol (3·2 g.), b. p. 124°/3 mm., n_D^{23} 1·5650 (lit.,[48] b. p. 132—143°/12 mm., n_D^{17} 1·5671). Chroman-4-ol was a gift from Professor O. Dann and had m. p. 44—45° and originated from Meerwein–Ponndorf reduction of chroman-4-one.[49]

(−)- and (±)-4′,5′-Dihydrodeguelin ("*β-Dihydrorotenone*").—Rotenone (5 g.) in pyridine (20 ml.) was hydrogenated over palladium–barium sulphate (2 g.) until 1 mol. of hydrogen had been absorbed. After filtration, the solution was diluted with much water, and the precipitate was extracted with ether. The ethereal solution was washed with 2N-alkali, the alkaline extracts were acidified, and the rotenonic acid was collected (0·7 g.); it had m. p. 206—210° (from methanol) (Found: C, 69·95; H, 6·1. Calc. for $C_{23}H_{24}O_6$: C, 69·7; H, 6·1%), $\lambda_{max.}$ 234 (4·18) and 292 (4·22) mμ, $\nu_{max.}$ 3333 (OH), 1669 (C=O), 1597 and 1502 cm.$^{-1}$ (aryl), $\nu_{max.}$ (mull) 1656 (C=O) cm.$^{-1}$ {lit.,[10] m. p. 206—208°, $[\alpha]_D$ +46° (in $CHCl_3$)}. Rotenonic acid (500 mg.) was dissolved in concentrated sulphuric acid (1·5 ml.) and glacial acetic acid (6 ml.), warmed for 15 min., and poured into water. The precipitate was filtered off, dissolved in chloroform, washed with 2N-alkali and water, dried, and recovered, giving (−)-4′,5′-dihydrodeguelin which, crystallised from a small volume of chloroform, had m. p. 155—156° (Found: C, 69·3; H, 6·0%), $[\alpha]_D^{19}$ −95·2° (*c* 3·9 in C_6H_6), $[\alpha]_D^{19}$ −22·6° (*c* 3·7 in $CHCl_3$), $\lambda_{max.}$ 234 (4·19) and 288 (4·28) mμ, $\nu_{max.}$ 1669 (C=O) cm.$^{-1}$, $\nu_{max.}$ (mull) 1672 (C=O) cm.$^{-1}$. Haller and LaForge [19,20] give m. p. 156°, $[\alpha]_D^{34}$ −26·5° (*c* 5·86 in $CHCl_3$), $[\alpha]_D^{20}$ −92·5° (*c* 2 in C_6H_6), for material made in this way and m. p. 155—156°, $[\alpha]_D^{20}$ −104° (*c* 4 in C_6H_6), for (−)-4′,5′-dihydrodeguelin from natural sources.

(−)-4′,5′-Dihydrodeguelin (600 mg.) was refluxed with potassium carbonate in acetone for 1½ hr. Working up in the usual way gave (±)-4′,5′-dihydrodeguelin (460 mg.), m. p. 173·5—174·5° (from methanol–chloroform) (Found: C, 69·25; H, 6·3%), $[\alpha]_D^{19}$ 0°, $\lambda_{max.}$ 234 (4·21) and 288 (4·30) mμ, $\nu_{max.}$ 1669 (C=O) cm.$^{-1}$. From the mother-liquors a second form, m. p. 155°, was isolated. The forms were interconverted by seeding and had the same infrared spectrum. The infrared spectra (mulls) of the specimen, m. p. 173·5—174·5°, and naturally derived (±)-4′,5′-dihydrodeguelin were identical. The infrared spectra of (−)- and (±)-4′,5′-dihydrodeguelin in chloroform were identical. Haller and LaForge [22a] give m. p. 171° for "(±)-β-dihydrorotenone," but report that one specimen softened at 171° and melted at 176°.

Reduction of (−)- and (±)-4′,5′-Dihydrodeguelin with Lithium Aluminium Hydride.—(*a*)

[47] (*a*) LaForge and Smith, *J. Amer. Chem. Soc.*, 1929, **51**, 2574; (*b*) Haller and Schaffer, *ibid.*, 1933, **55**, 3495.
[48] Brochet and Cornubert, *Compt. rend.*, 1921, **172**, 1499; *Bull. Soc. chim. France*, 1922, **31**, 1280.
[49] Dann, Volz, and Huber, *Annalen*, 1954, **587**, 16.

(−)-4′,5′-Dihydrodeguelin (430 mg.) in dry tetrahydrofuran was added to lithium aluminium hydride (70 mg.) in tetrahydrofuran (10 ml.), and the mixture was stirred under nitrogen for 2 hr. Ethyl acetate, water, and N-sodium potassium tartrate solution were added and the mixture was extracted with chloroform. The extract was dried and evaporated to give a gum which crystallised (330 mg.) when treated with methanol. These crystals appear to be solvated for they have m. p. 90° with frothing, and one crystallisation raised the m. p. to 155—157°. In two other runs the (−)-12-*hydroxy-compound* (IXe; R = H), m. p. 160°, was obtained immediately, from methanol; this m. p. was raised to 163·5—165° by further crystallisation (Found: C, 69·0; H, 6·35. $C_{23}H_{26}O_6$ requires C, 69·35; H, 6·55%); the alcohol had $[\alpha]_D^{25}$ −46·2° (*c* 2·4 in C_6H_6), $\lambda_{max.}$ 288 (3·82) mμ, $\nu_{max.}$ 1623, 1597, and 1499 cm.$^{-1}$ (aryl bands). The infrared spectrum (chloroform) of the whole crude product was closely similar to that of the purified material.

(±)-4′,5′-Dihydrodeguelin (890 mg.) was similarly reduced with lithium aluminium hydride (400 mg.) and gave the (±)-12-*hydroxy-compound* (IXe; R = H) [*trans*-arrangement of 12-hydroxyl to 12a-hydrogen], m. p. 177—178° (from methanol) (Found: C, 69·25; H, 6·55%), $\lambda_{max.}$ 228 (3·78) mμ. The infrared spectrum (chloroform) was identical with that of the (−)-compound.

(*b*) (−)-4′,5′-Dihydrodeguelin (600 mg.), dissolved in dry tetrahydrofuran (10 ml.), was refluxed under nitrogen for 15 min. with lithium aluminium hydride in tetrahydrofuran. Ethyl acetate, water, and N-sulphuric acid were added and the solution was extracted with chloroform. Drying and evaporation gave a gum which, when chromatographed on alumina (K1) and triturated with light petroleum, crystallised to give the (−)-12,12a-*olefin* (XXIe; R = H) (120 mg.), m. p. 177·5—179·5° (from chloroform–methanol), identical (mixed m. p. and infrared solution spectrum) with the specimen of $[\alpha]_D^{25}$ −122° (*c* 1·93 in C_6H_6) below, except for its rotation $[\alpha]_D^{20}$ −82° (*c* 1·44 in C_6H_6) (Found: C, 72·45; H, 6·3. $C_{23}H_{24}O_5$ requires C, 72·6; H, 6·35%).

(±)-4′,5′-Dihydrodeguelin (920 mg.) was dissolved in tetrahydrofuran (30 ml.) and heated under reflux for 1 hr. with lithium aluminium hydride (670 mg.) in tetrahydrofuran. The product was worked up as above to give, after crystallisation from methanol–chloroform, the (±)-12,12a-*olefin* (XXIe; R = H) (350 mg.), m. p. 184—185° (Found: C, 72·45; H, 6·55%). Its infrared solution spectrum was identical with that of the (−)-specimen recorded above.

Dehydration of the (−)-6aβ,12aβ-12α-*Hydroxy-compound* (IXe; R = H).—The (−)-hydroxy-compound (500 mg.) was heated for 1 hr. at 100° with pyridine (5 ml.) and phosphorus oxychloride (2 ml.), then poured on ice, and the whole was extracted with ether. The extract was washed with dilute hydrochloric acid, dried, and evaporated: the residual gum crystallised, having m. p. 169—171° (330 mg.) (from chloroform–methanol). Chromatography of this product from benzene on alumina (K1) gave the (−)-12,12a-olefin (XXIe; R = H) (see above), m. p. 177·5—179·5° (180 mg.) (from chloroform–methanol), $[\alpha]_D^{25}$ −122° (*c* 1·93 in C_6H_6), $\lambda_{max.}$ 254 (4·24), 258 (4·28), 264 (4·23), 361 (4·49), and 380 (4·45) mμ. Another preparation gave material of m. p. 176° but $[\alpha]_D^{22}$ −30° (*c* 1·42 in C_6H_6).

Low-pressure Catalytic Hydrogenation of 6a,12a-*Dehydro-6′,7′-dihydro-5′*(R)-*rotenone* (VIIIb).—The dehydro-compound [50] had m. p. 226—228° (Found: C, 69·7; H, 5·75. Calc. for $C_{23}H_{22}O_6$: C, 70·05; H, 5·6%), $\lambda_{max.}$ 240 (4·37), 280 (4·30), and 310 (4·19) mμ, $\nu_{max.}$ 1628 cm.$^{-1}$ (C=O) (lit., m. p. 228—230°). The ketone (500 mg.) in glacial acetic acid (100 ml.) was hydrogenated over Adams platinum (35 mg.) until 49 ml. of hydrogen (N.T.P.) had been absorbed. The mixture was filtered and evaporated, the gummy residue triturated with methanol (50 ml.), and unchanged ketone (21 mg.) filtered off. On concentration, the methanol solution gave crystals (294 mg.), m. p. 120—127°, $[\alpha]_D^{17}$ −64° (*c* 2 in C_6H_6) (positive Durham test).[51] Another crystallisation led to m. p. 130—135°. Both specimens had infrared spectra almost identical with " mutadihydrorotenone " (see below). Repeated crystallisation from benzene–methanol then gave (−)-6′,7′-dihydrorotenone (18 mg.), m. p. and mixed m. p. 213—214°, $[\alpha]_D^{19}$ −215° (*c* 2 in C_6H_6). An authentic specimen of the latter [47*b*] had m. p. 212°, $[\alpha]_D^{20}$ −222·5° (*c* 2 in C_6H_6), $\lambda_{max.}$ 237 (4·23) and 295 (4·28) mμ, $\nu_{max.}$ 1667 (C=O) cm.$^{-1}$.

In a second experiment the product from the dehydro-compound (500 mg.) was freed from unchanged material and poured into water. The whole solid product (411 mg.; negative ferric reaction) had $[\alpha]_D^{22}$ −21° (*c* 2 in C_6H_6) and still contained a little dehydro-compound.

[50] LaForge and Smith, *J. Amer. Chem. Soc.*, 1930, **52**, 1091.
[51] Jones and Smith, *Ind. Eng. Chem., Analyt.*, 1933, **5**, 75.

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When racemised at positions 6a,12a by means of sodium acetate in the usual way, the whole product had $[\alpha]_D^{24}$ −77°. (−)-6′,7′-Dihydrorotenone (100 mg.) was refluxed for 18 hr. with ethanol (25 ml.) containing sodium acetate (1 g.). The whole product, isolated by pouring of the mixture into water, had $[\alpha]_D^{20}$ −94·5° (*c* 2 in C_6H_6). Dann and Volz [37] report $[\alpha]_D^{20}$ −87° (in C_6H_6) for the equilibrium mixture. It does not follow that the latter is exactly a 1 : 1 mixture but a value of $[\alpha]_D$ −85·6° (in C_6H_6) can be calculated from 6′,7′-dihydrorotenone (6aβ,12aβ,5′β), $[\alpha]_D^{20}$ −222·5°, and 6′,7′-dihydroepirotenone (6aα,12aα,5′β), $[\alpha]_D$ +51·4°,[36] so that it is approximately so.

(±)- *and* (−)-6,6aβ,12,12aβ,4′,5′-*Hexahydro*-2,3-*dimethoxy*-6′,6′-*dimethyl*-4H-*pyrano*-(3′,2′-8,9)*rotoxen* (XXVe; R = H).—(a) *By hydrogenolysis of* 4′,5′-*dihydrodeguelin.* The (−)-ketone (Xe; R = H; 6aβ,12aβ) (210 mg.), was hydrogenated over Adams platinum (100 mg.) in acetic acid (15 ml.) until 2 mol. of hydrogen had been absorbed. After filtration, the solution was poured into water and extracted with ether. The extracts were washed with sodium carbonate solution and water, dried, and evaporated to a gum which crystallised from methanol (m. p. 117—120°; 95 mg.); there followed a second crop, m. p. 100—105° (95 mg.), with an infrared spectrum closely similar to that of the first. Crystallisation from methanol gave pure 12-*deoxy-compound* (XXVe; R = H; 6aβ,12aβ), m. p. 122—122·5° (Found: C, 72·4; H, 6·6. $C_{23}H_{26}O_5$ requires C, 72·25; H, 6·85%), $[\alpha]_D^{25}$ −115° (*c* 0·63 in C_6H_6), $\lambda_{max.}$ 288 (3·85) mμ, $\nu_{max.}$ 1621, 1595, and 1511 cm.$^{-1}$. Similarly the (±)-ketone (Xe; R = H) (260 mg.) gave, on hydrogenation, solid (250 mg.), m. p. 151—152° (150 mg., from methanol) (Found: C, 72·0; H, 7·0%), $\lambda_{max.}$ 288 (3·89) mμ, $\nu_{max.}$ 1621, 1595, and 1511 cm.$^{-1}$. The infrared spectrum (chloroform) was identical with that of the (−)-12aβ-form (as mulls there were recognisable differences) and the spectrum of the whole crude product was nearly identical with that of the pure compound.

(b) *By hydrogenolysis of the hydroxy-compound* (IXe; R = H). The (−)-hydroxy-compound (IXe; R = H; 6aβ,12aβ) (390 mg.) was hydrogenated over Adams catalyst (200 mg.) in acetic acid (15 ml.) until 1 mol. of hydrogen was absorbed. Working up gave a solid of m. p. 112—114° (332 mg.), raised by crystallisation from methanol to m. p. 122° (150 mg.), $[\alpha]_D^{25}$ −115° (*c* 1·6 in C_6H_6), identical with the (−)-specimen described in (a) above. The spectrum of the crude whole product was identical with that of the purified material, and the stability of the (−)-hydroxy-compound towards dehydration under the reaction conditions was checked.

Similarly, the (±)-hydroxy-compound (109 mg.) on hydrogenolysis gave a glass (105 mg.) which, crystallised from methanol, had m. p. 151° (55 mg.), identical with the (±)-material described in paragraph (a).

(c) *By catalytic hydrogenation of the* (±)- *and* (−)-12,12a-*dehydro*-6aβ-*compound* (XXIe; R = H). The 12,12a-dehydro-compound (116 mg.; $[\alpha]_D^{22}$ −30°) was hydrogenated over Adams catalyst (80 mg.) in acetic acid (10 ml.) until 1 mol. of hydrogen had been absorbed. Working up gave a glass (107 mg.), $[\alpha]_D^{17}$ −24° (*c* 1·06 in C_6H_6), which when carefully crystallised gave the deoxy-compound (XXVe; R = H) in (±)-form, m. p. 149·5—150·5° (50 mg.), $[\alpha]_D$ 0°: mixed m. p. and infrared comparison established identity with the material described above. There followed a crop, m. p. 134—138° (15 mg.), $[\alpha]_D^{17}$ −2·5° (*c* 0·89 in C_6H_6), and finally a crop, m. p. 110° (8 mg.), $[\alpha]_D^{17}$ −106° (*c* 0·58 in C_6H_6). The infrared spectrum (mull) of the latter was indistinguishable from that of the (−)-form above, but this specimen was not optically pure. Infrared examination of the original glass gave no evidence of products other than the (−)- and (±)-compound (XXVe; R = H).

Similar hydrogenation of the (±)-12,12a-dehydro-compound (102 mg.) gave a gum which crystallised from methanol, to give the (±)-compound (XXVe; R = H), m. p. 149—150° (50 mg.), identical (mixed m. p. and infrared criteria) with the specimen just noted. No second compound could be traced in the crude product.

Reduction of 6a,12a-*Dehydrorotenone with Lithium Aluminium Hydride.*—The ketone (2 g.) in dry dioxan was heated with lithium aluminium hydride (1 g.), added in portions. After 1 hour's refluxing, the product was cooled, 2N-sulphuric acid was added, and the mixture was extracted with chloroform. The extracts were dried and evaporated, and the gum was chromatographed on alumina (N) to give, after crystallisation from benzene–methanol, the 12,12a-dehydro-compound (XXIa) (150 mg.), m. p. and mixed m. p. 164—165° with the specimen described below.

The 12,12a-*Dehydro-compound* (XXIa).—The hydroxy-compound (IXa; glass) (700 mg.) in dry pyridine (5 ml.) was heated at 100° with phosphorus oxychloride (2 ml.) for 1¼ hr. and

then poured on ice. Extraction with ether gave the dehydro-compound (XXIa) (510 mg.), which crystallised from benzene–light petroleum (b. p. 40—60°), m. p. 163—164° (Found: C, 73·05; H, 6·00. Calc. for $C_{23}H_{22}O_5$: C, 73·0; H, 5·85%), $[\alpha]_D^{23}$ −272·5° (*c* 2 in C_6H_6), $\lambda_{max.}$ 255 (4·15), 265 (4·12), 360 (4·47), and 375 (4·41) mμ (lit.,[16] m. p. 160—161°).

(−) - 6,6aβ,12,12aβ,4′,5′ - *Hexahydro* - 2,3 - *dimethoxy* - 5′β - *isopropylfurano*(3′,2′ - 8,9)*rotoxen* (XXVb).—(a) *By hydrogenolysis of rotenone.* Rotenone (1 g.) in glacial acetic acid (20 ml.) was hydrogenated over Adams catalyst (250 ml.) until 3 mol. of hydrogen had been absorbed. Working up gave the deoxy-compound (XXVb) (650 mg.), m. p. 172—173° (from ethanol) (Found: C, 72·0; H, 7·0. $C_{23}H_{26}O_5$ requires C, 72·25; H, 6·85%), $[\alpha]_D^{22}$ −150·5° (*c* 2 in $CHCl_3$), $\lambda_{max.}$ 290 (3·88) mμ, $\nu_{max.}$ 1616, 1602, and 1500 cm.$^{-1}$. The same compound (m. p. and mixed m. p. 175°) was also obtained by reduction of rotenone in ethyl acetate over Adams catalyst at 50°/30 atm. for 7 days. Butenandt [38] gives m. p. 168°.

(b) *By hydrogenolysis of the hydroxy-compound* (IXa). The glass (500 mg.) obtained by reducing rotenone with lithium aluminium hydride was hydrogenated in acetic acid (10 ml.) over Adams catalyst (100 mg.) until 2 mol. of hydrogen had been absorbed. Working up gave the above deoxy-compound, m. p. 173—174° (300 mg.), $[\alpha]_D^{27}$ −150° (*c* 2 in $CHCl_3$). Crystalline hydroxy-compound (IXa; methanol solvate) (15 mg.) similarly hydrogenated gave the same compound, m. p. and mixed m. p. 173°.

(c) *By hydrogenolysis of the enol-acetate* (XXIIa). The enol-acetate (200 mg.) was hydrogenated as above (3 mol. of hydrogen). Working up gave the above deoxy-compound (90 mg.), m. p. 172°, $[\alpha]_D^{28}$ −148° (*c* 2 in $CHCl_3$).

(d) *By hydrogenation of the* 12,12a-*dehydro-compound* (XXIa). Hydrogenation of the dehydro-compound (300 mg.) as above (2 mol. of hydrogen) gave the deoxy-compound (XXVb) (200 mg.), m. p. 172° (Found: C, 72·25; H, 7·05%; *M*, 394), $[\alpha]_D^{22·5}$ −128·2° (*c* 2 in $CHCl_3$), $\lambda_{max.}$ 290 (3·80) mμ. It did not depress the m. p. of samples of $[\alpha]_D$ −150° and had an identical infrared solution spectrum.

2-(2,4,5-*Trimethoxyphenyl*)*ethanol.*—2,4,5-Trimethoxyphenylacetic acid was made from derritol according to a published degradation sequence [52] and reduced with lithium aluminium hydride in the usual way. Working up gave an alcohol, b. p. 163°/0·06 mm., m. p. 75—76° (from benzene–light petroleum) (Found: C, 61·6; H, 7·85. Calc. for $C_{11}H_{16}O_4$: C, 62·25; H, 7·6%). Apart from the three infrared clear bands, mentioned in the text, a very weak maximum near 3500 cm.$^{-1}$ has been observed: its origin is not known.

3,4-*Dimethoxybenzyl Alcohol.*—Prepared by reduction of veratraldehyde with potassium borohydride this had b. p. 240°/40 mm., n_D^{20} 1·554, m. p. 54° (lit.,[53] b. p. 172°/12 mm., n_D^{17} 1·555).

2-(3,4-*Dimethoxyphenyl*)*ethanol.*—Reduction of 3,4-dimethoxyphenylacetic acid, m. p. 99° (lit.,[53] m. p. 98—99°), with lithium aluminium hydride gave 2-(3,4-dimethoxyphenyl)ethanol, m. p. 46° (lit.,[54] m. p. 47—48°).

(+)-*Isorotenone.*—" *d*-Epirotenone " concentrate [10] {20 g; $[\alpha]_D^{18}$ +25° (*c* 2 in C_6H_6)} in glacial acetic acid (200 ml.) was treated dropwise with concentrated sulphuric acid (150 ml.), the temperature being kept below 65°, and the red product was poured into water. The precipitated solid (17 g.) crystallised from ethanol, to give (+)-6aα,12aα-isorotenone, m. p. 183—184°, $[\alpha]_D^{18}$ +82° (*c* 2 in C_6H_6) {lit.,[10] m. p. 182°, $[\alpha]$ +75° (in C_6H_6)}. When crystallised with (−)-isorotenone, this gave (±)-isorotenone, m. p. and mixed m. p. 172—173°.

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(G. B. and J. S. K.) Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Mass., U.S.A.
(L. C., P. J. G., K. S. S., D. A. W.) University of London King's College, Strand, London, W.C.2.
Imperial College of Science and Technology, South Kensington, London, S.W.7.

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554. *The Structure and Stereochemistry of the Rotenolones, Rotenolols, Isorotenolones, and Isorotenolols.**

By L. Crombie and P. J. Godin.

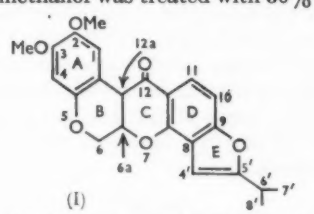
(±)-Isorotenolone A and B, formed by alkaline oxygenation of (−)-isorotenone, are *cis*- and *trans*-12a-hydroxy-derivatives respectively. Optically active forms are made by oxidation with dichromate in acetic acid, and their absolute stereochemistry is established. Reduction of (±)-isorotenolone A (*cis*-B/C) gives one (±)-diol, whilst (±)-isorotenolone B (*trans*-B/C) gives two. The configurations of these are established, and the work is extended to deal with the absolute stereochemistry of corresponding optically active diols. The stereochemistry of (±)-tephrosin and (±)-isotephrosin is also elucidated.

Alkaline oxygenation of natural rotenone gives four diastereoisomers (all 5′β), instead of the two racemates above. By direct and indirect means these are isolated and stereochemically identified. The absolute stereochemistry of their reduction products is then worked out.

(±)-Isorotenolone C which results when (−)-isorotenone is treated with alkaline hydrogen peroxide is the spiro-hydroxy-compound (XXXIV).

The isorotenolones, four racemic hydroxy-derivatives of (±)-isorotenone (I), were investigated by LaForge and Haller[1] but they were unable to propose definite structures. In this paper the status of the four compounds is examined, structural and stereochemical proposals are made, and the treatment is then extended to optically active isorotenolones. Later, the more complex case of the rotenolones is cleared up and stereochemical work is developed to deal with the diols produced by reduction of the isorotenolones and rotenolones (isorotenolols and rotenolols).

LaForge and Haller[1] listed isorotenolones I (m. p. 203—204°), II (m. p. 193—194°), C (m. p. 210—212°) and D (m. p. 188—189°). The first two can be made by aerating an alkaline suspension of isorotenone; isorotenolone I is also obtained when (±)-12a-acetoxyisorotenone (IIc; R′ = OAc),† which is isolated together with 6a,12a-dehydroisorotenone (IIIc) when (−)- or (±)-isorotenone is treated with iodine and sodium acetate, is hydrolysed. Isorotenolone C and D were encountered when (−)- or (±)-isorotenone in alkaline methanol was treated with 30% aqueous hydrogen peroxide.



(I) (II)† (III)

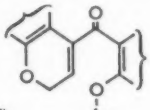
† In order to conserve space, the letter following the Roman numeral indicates that the complete structural series to which the compound belongs is as follows: a, 5′β-rotenone; b, 6′,7′-dihydro-5′β-rotenone; c, isorotenone; d, deguelin (R = H) or toxicarol (R = OH); e, 4′,5′-dihydrodeguelin (R = H) or 4′,5′-dihydrotoxicarol (R = OH); f, 6a,12a-dihydro-6*H*-rotoxen-12-one; g, dihydrorotenonic acid (1′,5′-*seco*); h, rotenonic acid (1′,5′-*seco*). The omitted pieces of the structures are on p. 2846.

Pure isorotenolone I has m. p. 208—209° and is now referred to as (±)-isorotenolone A. The preparation[1] of isorotenolone II is reproducible, but the product of m. p. 193—194° is a mixture of (±)-isorotenolone A and a new isomeric hydroxy-derivative, m. p. 243°, namely, (±)-isorotenolone B. The mixture of (±)-isorotenolone A and B can also be made by treating the 6a,12a-dehydro-6a,7-*seco*-acetate (IVc) with t-butyl hydroperoxide and Triton B, and has been encountered in the treatment of isorotenone with alkaline

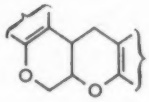
* For a preliminary communication see Crombie and Godin, *Proc. Chem. Soc.*, 1960, 276.

[1] LaForge and Haller, *J. Amer. Chem. Soc.*, 1934, **56**, 1620.

hydrogen peroxide. Hydrolysis of crystalline (±)-12a-acetoxyisorotenone gives, besides (±)-isorotenolone A, a little (±)-isorotenolone B. LaForge and Haller reported that oxidation of isorotenone with alkaline peroxide gave mainly (±)-isorotenolone C with only small quantities of D. Careful search of a number of preparations revealed no (±)-isorotenolone D, only C (m. p. 211—212°). But on one occasion the whole product had m. p. 189—190° in agreement with that reported for D; this compound is, however, only a polymorph of C, for although its spectrum as a mull differs slightly, in solution it is identical with that of C; also the low-melting form reverted to the high-melting form after one crystallisation from chloroform–methanol. The existence of isorotenolone D is thus doubtful but it must be pointed out that LaForge and Haller state that their specimen gave a methyl ether different from that of C. It will emerge that isorotenolones A and B are based on an unaltered isorotenone skeleton, whereas C involves a spiro-system. Although (−)-isorotenone can be used as a starting material in the above preparation, the isorotenolones obtained are (±)-compounds because the basic conditions racemise centres 6a and 12a. Nonetheless, optically active forms of isorotenolone A and B can be made in another way and are discussed below.

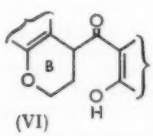


(IV)



(V)

The hydroxyl group in (±)-isorotenolone A and B is located on the B/C ring junction since brief refluxing with 10% sulphuric acid converts either into 6a,12a-dehydroisorotenone (IIIc): also neither ketol is dehydrogenated by active manganese dioxide under conditions which readily give 6a,12a-dehydroisorotenone from isorotenone. Specifically, the 12a-position is implicated by the absence of enolisation reactions. Thus only a monoacetyl derivative is formed under conditions which, if there were a 12a-hydrogen atom, would lead to a diacetyl derivative (one enol acetate group). The preparation of (±)-acetylisorotenolone A by the iodination technique, or by treatment of (±)-isorotenone with lead tetra-acetate, also indicates substitution at position 12a. The conversion of (±)-isorotenolone B methyl ether into the corresponding A compound, and the formation of (±)-acetylisorotenolone A when (±)-isorotenolone B is acetylated, have been mentioned earlier.[2] (±)-Isorotenolone A and B are thus represented by (IIc; R′ = OH). In agreement, vigorous catalytic hydrogenation produces either the bis-deoxygenated compound (Vc) or (Vb) by hydrogenolysis of one actual and one potential benzylic hydroxyl group. When treated with zinc and alkali, (±)-isorotenolone A and B each give isorotenol (VIc) and isoderritol (VIIc): this is as expected since the 12a-hydroxyl group is eliminated as in (VIIIc) and degradation as explained elsewhere [3] ensues.



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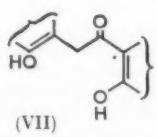
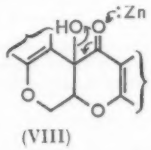


(VII)



(VIII)

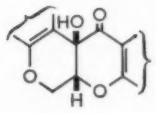
(±)-Isorotenolone A and B must be represented by one or other of the *cis*-B/C racemate (IX—Xc) or the *trans*-B/C racemate (XI—XIIc), and the immediate problem is to assign the correct fusion to each compound.

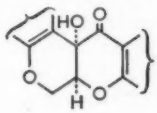
(±)-Isorotenolone B, which is dehydrated by acid rather faster than A, is less soluble than A in most solvents, including carbon tetrachloride, and infrared examination indicates intramolecular hydrogen bonding of only a very weak kind. In fairly concentrated

[2] Büchi, Crombie, Godin, Kaltenbronn, Siddalingaiah, and Whiting, preceding paper.
[3] Crombie, Godin, Siddalingaiah, and Whiting, following paper.

XUM

solution (*ca.* 5%) a free or lightly bonded hydroxyl group is indicated by absorption at 3610 (±10) cm.$^{-1}$, and a strong intermolecular-bonding band at ~3310 cm.$^{-1}$ (broad) (NaCl, $CHCl_3$). In dilute solution only a lightly bonded hydroxyl group is revealed, at 3593 cm.$^{-1}$ (LiF, CCl_4 < ~0·005M). (±)-Isorotenolone A has, in fairly concentrated solution, an intramolecularly bonded hydroxyl at 3497 (± ~10) cm.$^{-1}$ (NaCl,$CHCl_3$) and shows no intermolecular bonding. In dilute solution the situation is virtually unchanged, with only an intramolecularly bonded hydroxyl at 3506 cm.$^{-1}$ (LiF, CCl_4 < ~0·005M).


(IX)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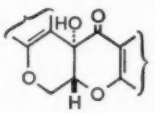
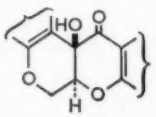
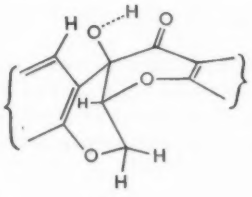

(XI)


(XII)

For the A isomer the strength of the intramolecular bond is considerably greater than expected for aryl or ether bonding [4] in a molecule such as (±)-isorotenolone and suggests that the ketone group must be involved. This is confirmed: whereas the ketone stretching vibration in (±)-isorotenolone B (1697 cm.$^{-1}$) is higher than that of its methyl ether (1688 cm.$^{-1}$) or the parent ketone (I) (1677 cm.$^{-1}$), in (±)-isorotenolone A (1676 cm.$^{-1}$) it is lowered relative to that of its methyl ether (1683 cm.$^{-1}$) (CaF_2, $CHCl_3$). Hydrogen bonding to a ketone group is known to lower the stretching frequency.[5] In (±)-*trans*-isorotenolone (XV) the hydroxyl group is badly oriented towards the ketonic oxygen and the situation is similar in one *cis*-conformation (XIII). The other *cis*-conformation (XIV)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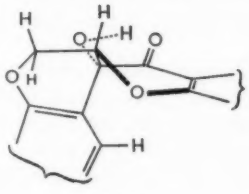
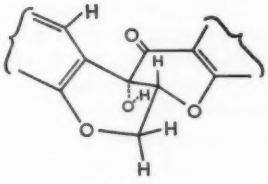

(XIV)


(XV)

has the hydroxyl group approaching co-planarity with the carbonyl lone-pair orbitals,[6] and the hydroxyl-hydrogen atom is closer to the oxygen atom than in (XIII) or (XV). This satisfactorily accounts for the intramolecular bond in (±)-isorotenolone A. In agreement, the ketol (XVI), in which there is a very similar relationship (XVII) between the ketone and the hydroxyl group to that in (XIV), shows the hydroxyl frequency at 3500 cm.$^{-1}$ (CS_2).[7] (±)-Isorotenolones A and B are thus assigned *cis*- and *trans*-fusions respectively.

(±)-Tephrosin and (±)-isotephrosin [8] result when (±)-deguelin (XVIII; R = H) is aerated in alkaline solution. On dehydration, both give 6a,12a-dehydrodeguelin (IIId; R = H) and their reactions in general parallel those of (±)-isorotenolones A and B. By applying the above spectroscopic criteria, (±)-tephrosin is assigned the *cis*-B/C fusion (IX—Xd; R=H) since it possesses the intramolecularly bonded hydroxyl group [3498 (CaF_2, CCl_4; < ~0·005M) and 3509 cm.$^{-1}$ (NaCl, $CHCl_3$; ~5%)] and ketone (1675 cm.$^{-1}$; cf. deguelin,

[4] *Inter al.*, Fales and Wildman, Abs. Amer. Chem. Soc. 138th Meeting, Sept. 11–16, 1960, p. 19P; Brimacombe, Foster, Stacey, and Whiffen, *Tetrahedron*, 1958, **4**, 351; Barker, Brimacombe, Foster, Whiffen, and Zweifel, *Tetrahedron*, 1959, **7**, 10; Kuhn, *J. Amer. Chem. Soc.*, 1958, **80**, 5950, and earlier papers.

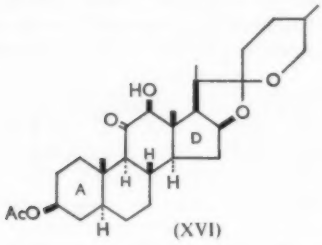
[5] Cole and Müller, *J.*, 1959, 1224; Pickering and Werbin, *J. Amer. Chem. Soc.*, 1958, **80**, 680.

[6] Schneider, *J. Chem. Phys.*, 1955, **23**, 26.

[7] Elks, Phillipps, Walker, and Wayman, *J.*, 1956, 4330.

[8] (*a*) Clark, *J. Amer. Chem. Soc.*, 1931, **53**, 729; (*b*) Clark and Claborn, *ibid.*, 1932, **54**, 4454; (*c*) Clark, *ibid.*, 1943, **65**, 27; (*d*) Boam, Cahn, and Stuart, *J. Soc. Chem. Ind.*, 1937, 91T.

1669 cm.$^{-1}$). (±)-Isotephrosin has a free (3597 cm.$^{-1}$) and intermolecularly bonded hydroxyl group (3311 cm.$^{-1}$, broad) in chloroform solution (NaCl), and its 12-ketone vibration is at 1695 cm.$^{-1}$: it is less soluble than (±)-tephrosin in carbon tetrachloride. These facts are consistent with the *trans*-B/C assignment (XI—XIId; R = H).



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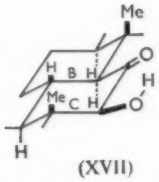
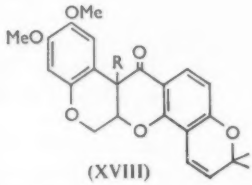


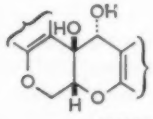
(XVII)



(XVIII)

The key to the preparation of optically active isorotenolones is contained in a paper by Clark who noticed that treatment of (±)-toxicarol with dichromate in acetic acid gave a (±)-hydroxytoxicarol.[9] When applied to (−)-6aβ,12aβ-isorotenone, this reagent gave two 12a-hydroxy-compounds; because of the acid conditions the 6a-centre is not racemised. The first product, m. p. 97° (methanol solvate), $[\alpha]_D^{16}$ −52° (in $CHCl_3$), has a *cis*-B/C junction (infrared criteria) and is thus ketol (IXc). The second, m. p. 220°, $[\alpha]_D^{19}$ +366° (in $CHCl_3$), formed in small yield, is much less soluble and as again the configuration at position 6a is β, it is the ketol (XIc), in agreement with infrared data. Similar oxidation of (+)-6aα,12aα-isorotenone [2,10] gave the *cis*-isorotenolone (Xc), m. p. 96° (methanol solvate), $[\alpha]_D^{16}$ +53° (in $CHCl_3$), enantiomorphic with (IXc). When crystallised together, the enantiomorphs gave (±)-isorotenolone A.

The diols obtained by reducing isorotenolones with borohydride will next be considered. (±)-Isorotenolone B gave two diols, (±)-B_1, m. p. 263°, and (±)-B_2, m. p. 213°. The *trans*-B/C junction must be maintained and one must have a *cis*- and the other a *trans*-12,12a-diol arrangement. Because it is cleaved almost instantly with lead tetra-acetate, and because it results when the 12,12a-unsaturated racemate (XXVII—XXVIIIc) is



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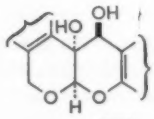

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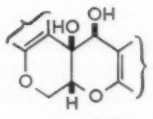
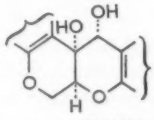


(XXI)



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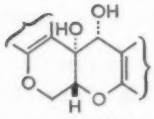

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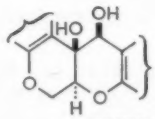

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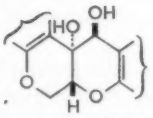

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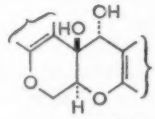


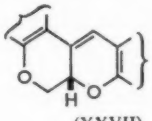
(XXVI)

cis-hydroxylated with osmium tetroxide, the (±)-B_1-diol must be the *cis*-12,12a-diol racemate (XXIII—XXIVc). The (±)-B_2-diol is thus the *trans*-12,12a-racemate (XXV—XXVIc) and, as expected, reacts more slowly with lead tetra-acetate. Both diols (±)-B_1 and (±)-B_2 re-formed (±)-isorotenolone B when treated with manganese dioxide, showing that the B/C fusion is unaltered. When (±)-isorotenolone A (IX—Xc), with a *cis*-B/C fusion, was reduced either by borohydride or catalytically, only one diol, (±)-A, m. p. 218°, was isolated. This reacted with lead tetra-acetate more slowly than the *cis*-12,12a-diol

[9] Clark, *J. Amer. Chem. Soc.*, 1934, **56**, 987.
[10] Cahn, Phipers, and Boam, *J.*, 1938, 513.

(±)-B_1, though faster than the (±)-B_2-diol. Structure (XIX—XXc) is consistent with this as (XXI—XXIIc) would react almost instantaneously. On oxidation with manganese dioxide, the (±)-A-diol formed (±)-isorotenolone A. This formation of racemate (XIX—XXc) alone or dominantly is as expected, for the α-face in rotenone and derivatives with *cis*-B/C fusion (XIII—XIVc) is hindered and attack by borohydride ion or catalytic hydrogenation would give predominantly an α-oriented hydroxyl at position 12. The *trans*-B/C fusion is open to attack from each face. Diols (±)-A and B_1 each gave (±)-isorotenone, presumably by intervention of the 12a-carbonium ion, when treated with acid.

Similar work has been carried out on optically active *cis*-B/C isorotenolones. Thus the 6aβ,12aβ-ketol (IXc) gave the 12α-diol (6aβ,12aβ; XIXc), m. p. 176°, $[\alpha]_D^{20}$ −157° (in $CHCl_3$) whilst the 6aα,12aα-ketol (Xc) gave the 12β-diol (6aα, 12aα; XXc), m. p. 176°, $[\alpha]_D^{20}$ +160° (in $CHCl_3$). Crystallised together, the two enantiomorphs formed the (±)-diol A, m. p. 218°. Each of the racemic diols (±)-A, (±)-B_1, and (±)-B_2 could be degraded to the same racemic keto-aldehyde (XXIX—XXXc), m. p. 182°, when treated with periodic acid in aqueous methanol. Effectively the (±)-B_2-racemate resembles a diaxial diol and it seems likely that the cleavage is preceded by acid-catalysed epimerisation at position 12a. The enantiomorphs (XXIXc), m. p. 190°, $[\alpha]_D^{21}$ +205° (in $CHCl_3$), and (XXXc), m. p. 190°, $[\alpha]_D^{21}$ −202° (in $CHCl_3$), were obtained by treating the diols (XIXc) and (XXc) with periodic acid.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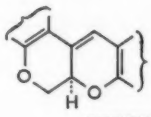
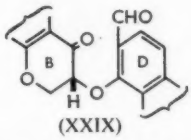
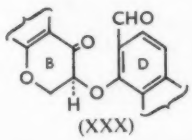

(XXVIII)

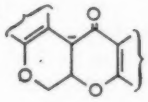


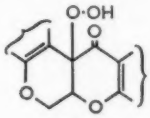
(XXIX)



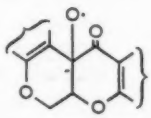
(XXX)

In the absence of definite information, the formation of isorotenolones by aerial oxidation in alkaline medium can be viewed as resulting from attack by molecular oxygen on the ion (XXXIc) to give hydroperoxide ion. The hydroperoxide (XXXIIc) thus formed may react with ion (XXXIc) or with hydroxyl ion [11] to give an isorotenolone, or, less probably, may break down homolytically to (IIc; R′ = OH) *via* the radical (XXXIIIc).


(XXXI)



(XXXII)



(XXXIII)

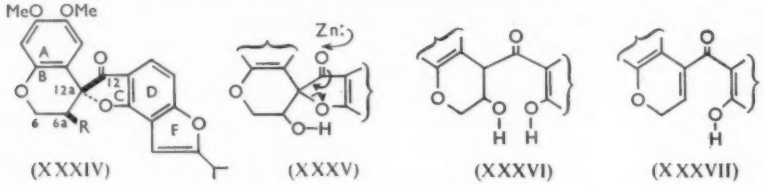
(±)-Isorotenolone C is made by heating a solution of (−)-isorotenone in 5% methanolic potassium hydroxide with 30% hydrogen peroxide at 60°: conditions are rather critical. Analogous compounds can be obtained from deguelin [1] and from dihydrorotenone. (±)-Isorotenolone C is isomeric with A and B and contains one hydroxyl group (Zerewitinoff) which forms a methyl ether, a toluene-*p*-sulphonate and, by treatment with keten or refluxing sodium acetate–acetic anhydride, a monoacetate. The latter conditions gave an enol acetate when applied to isorotenone, so position 12a probably carries no hydrogen atom: this is supported by the failure to iodinate (±)-isorotenolone C. The compound is insoluble in alkali, gives no ferric reaction, and is not methylated on prolonged contact with diazomethane, and its acetate has its C–O stretching frequency at 1230 $cm.^{-1}$ (in acetonitrile). These facts suggest that the hydroxyl group is not aromatic (aromatic acetates absorb near 1205 $cm.^{-1}$, steroid acetates near 1240 $cm.^{-1}$). A benzylic placing is not satisfactory as the compound is not oxidised by manganese dioxide or catalytically hydrogenolysed under rather severe conditions. Dehydration is difficult.

[11] Howe and McQuillen, *J.*, 1958, 1513.

XUM

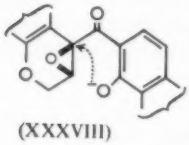
The infrared spectrum of (±)-isorotenolone C shows an intermolecularly bonded hydroxyl at 3378 cm.$^{-1}$ (NaCl, $CHCl_3$) and in dilute solution a " free " (3609 cm.$^{-1}$) and a bonded (3578 cm.$^{-1}$) hydroxyl group (LiF, CCl_4; $< \sim 0{\cdot}005$M). Compared with that of isorotenone (1680 cm.$^{-1}$), the ketone frequency for (±)-isorotenolone C (1706 cm.$^{-1}$) suggests that it is in a five-membered environment. A relationship with the spiro-compound (XXXIV; R = H) ($\nu_{max.}$ 1709 cm.$^{-1}$), the structure of which is dealt with elsewhere,[3] is at once suggested and is supported by the close similarity of their ultraviolet spectra (which are virtually unchanged by acid or alkali). As required, position 12a is blocked. The formation of analogues from deguelin and dihydrorotenone makes it highly unlikely that ring E or its addendum carries the hydroxyl group: this leaves only positions 6 and 6a. In the former case the compound would be a hemiketal, but (±)-isorotenolone C shows none of the expected properties. When treated with phosphorus oxychloride in pyridine it forms a chloro-derivative which is very stable to base and is thus much more in accord with a β- than an α-halogeno-ether formulation.

In agreement with (XXXIV; R = OH; and enantiomorph), (±)-isorotenolone C gives isorotenol (VIc) and isoderritol (VIIc) when treated with zinc and alkali. This is readily



(XXXIV) (XXXV) (XXXVI) (XXXVII)

explained by attack as in (XXXVc) to give the β-hydroxy-compound (XXXVIc) which can yield the first intermediate (XXXVIIc) of the rotenol–derritol change discussed later.[3] (±)-Isorotenolone C is reduced to a diol by borohydride: as expected, oxidation of this diol with manganese dioxide gives back the original ketol. The formation of (±)-isorotenolone C from (−)-isorotenone may be viewed as attack by $^{-}$O·OH on the ion of (XXXVIIc), which is available in an alkaline solution of isorotenone,[3] to give an epoxide[12] which is attacked intramolecularly as in (XXXVIIIc).[12b] Consequently the hydroxyl group may be *cis*- to the keto-group in the spiro-system. It is not optimally placed for bonding to the ketone, so the hydroxyl stretching frequency (above) does not necessarily conflict with this stereochemistry.



(XXXVIII)

Takei and his colleagues[13] have reported that alkaline oxygenation of natural (−)-rotenone gives two products, rotenolone I, m. p. 137—138°, and rotenolone II, m. p. 210°, and this has been confirmed by Miyano and Matsui.[14] These compounds are accepted by them as individuals: but because there is an optical centre at 5′(β) four diastereoisomeric ketols (IX—XIIa) must be produced instead of the two pairs of enantiomorphs (IX—Xc) and (XI—XIIc) obtained when isorotenone is similarly treated. The two expected *trans*-B/C ketol diastereoisomers, 6aβ,12aα,5′β (XIa), m. p. 251°, $[\alpha]_D^{15}$ +420° (in $CHCl_3$), and 6aα,12aβ,5′β (XIIa), m. p. 212°, $[\alpha]_D^{19}$ −78° (in $CHCl_3$), could in fact be separated by fractional crystallisation of the higher-melting and less soluble rotenolone II. As the mixture of *cis*-B/C ketol diastereoisomers contained in rotenolone I did not part cleanly on crystallisation, they were made in another way (the presence of the two diastereoisomers in rotenolone I was, however, shown indirectly by examination of the products obtained by reduction with borohydride). The 6aβ,12aβ,5′β (IXa) compound, m. p. 88° (methanol solvate), $[\alpha]_D^{16}$ −189° (in $CHCl_3$), was the major product when natural rotenone was treated

[12] (*a*) Payne, *J. Org. Chem.*, 1958, **23**, 310; (*b*) Vander Werf, Heisler, and McEwen, *J. Amer. Chem. Soc.*, 1954, **76**, 1231.
[13] Takei, Miyajima, and Ono, *Ber.*, 1933, **66**, 482.
[14] Miyano and Matsui, *Chem. Ber.*, 1959, **92**, 1438.

with dichromate–acetic acid, whilst the 6aα,12aα,5′β (Xa) diastereoisomer was formed by similar treatment of an epirotenone [10] concentrate. The second ketol was amorphous, $[\alpha]_D^{18}$ +26° (in $CHCl_3$), but yielded crystalline degradation products (below). Assignment of structure to these compounds rests on criteria similar to those used for isorotenolones above and emerges in the degradations below. Assignment of ring fusion depends on hydroxyl-to-ketone hydrogen-bonding criteria. The configuration of the two *cis*-B/C diastereoisomers at 6a is apparent from that of their precursors, whilst that of the two *trans*-B/C diastereoisomers at this centre is shown below by degradation. In all four compounds the configuration (β) at 5′ remains the same.

As in the case of the isorotenolones, each *trans*-B/C rotenolone diastereoisomer gave a separable pair of 12,12a-diols when reduced with borohydride. Thus the 6aβ,12aα,5′β-ketol (XIa) gave the 6aβ,12aα,12α,5′β-diol (XXIIIa) and the 6aβ,12aα,12β,5′β-diol (XXVa), whilst the 6aα,12aβ,5′β-ketol (XIIa) gave the 6aα,12aβ,12β,5′β-diol (XXIVa) and the 6aα,12aβ,12α,5′β-diol (XXVIa). The *cis*-12,12a-diol structure is assigned to compounds (XXIIIa) and (XXIVa) because they are cleaved almost instantaneously with lead tetra-acetate, whilst reaction of the *trans*-12,12a-diols (XXVa) and (XXVIa) is considerably slower. On preparative cleavage with periodic acid the diols (XXIIIa) and (XXVa) gave the keto-aldehyde (XXIXa) of known β-configuration at positions 6a and 5′ (below), whilst the diols (XXIVa) and (XXVIa) gave the keto-aldehyde (XXXa) of known α-configuration at 6a and β at 5′ (below). These diols were oxidised back to their parent ketols by manganese dioxide, and the information given allows complete definition of their stereochemistry.

Only one diol was isolated from each of the two *cis*-B/C rotenolone diastereoisomers on reduction with borohydride. The 6aβ,12aβ,5′β-ketol (IXa) gave the 6aβ,12aβ,12α,5′β-diol (XIXa) (methanol solvate), and the 6aα,12aα,5′β-ketol (Xa) gave the 6aα,12aα,12β,5′β-diol (XXa) (methanol solvate).* The *trans*-12,12a-diol arrangement is assigned to each because, although they are cleaved more rapidly than the " *trans*-diaxial " diols, the rate is considerably slower than that of the *cis*-12,12a-diols above. The configurations at positions 6a and 5′ follow from the stereochemistry of their precursors, and thus the configurations of the keto-aldehyde (XXIXa) (6aβ,5′β) isolated by periodate treatment of diol (XIXa), and the keto-aldehyde (XXXa) (6aα,5′β) similarly isolated from diol (XXa), are known. These are the reference substances used above.

In a recent paper by Miyano and Matsui [14] assignments for the rotenolones and rotenolols were made, but differently from those above. Experimental differences apart, our interpretations diverge on the following main points. First, we recognise four diastereoisomeric ketols obtained on alkaline oxygenation of rotenone, not two (these are mixtures). Secondly, our assignments of configuration to the B/C fusions are opposite to those claimed. Thirdly, the stereochemical position regarding the rotenolols does not seem to be properly appreciated by Miyano and Matsui—a total of eight forms is possible with the natural configuration at 5′. In two cases, because in our submission their interpretation is incorrect, Miyano and Matsui have to postulate an unexpected epimerisation at position 6a during borohydride reduction. This, they admit, they do not understand, and no such epimerisations are required in our treatment. Recent assignments [14,15] to tephrosin and isotephrosin also differ from ours above. Biological evidence cited [16] in favour of a *trans*-B/C configuration for " rotenolone I," if accepted as valid, is just as easily interpreted in favour of a *cis*-B/C configuration, for it suggests only that " rotenolone I " [*i.e.*, (IXa) and (Xa)] and natural rotenone possess the same B/C fusion.

* Among the rotenolols, pairs which would be enantiomorphic but for the possession by each of the same 5′β-isopropenyl group, have virtually indistinguishable solution spectra, *e.g.*, (XIXa)–(XXa), (XXIIIa)–(XXIVa), and (XXVa)–(XXVIa). In other cases the diastereoisomers have distinctly different solution spectra.

[15] Miyano, Nishikubo, and Matsui, *Chem. Ber.*, 1960, **93**, 1746.
[16] Miyano and Matsui, *Bull. Agric. Chem. Soc. Japan*, 1958, **22**, 335.

XUM

Experimental

For general working procedures see the preceding paper.

Preparation of (±)-*Isorotenolone A and B by Alkaline Oxygenation.*—(−)-Isorotenone (18 g.) was suspended in ethanol (450 ml.) containing N-aqueous potassium hydroxide (15 ml.), and a rapid stream of air was passed through the mixture for 6 hr. Next morning a granular precipitate (13 g.) was obtained which crystallised as prisms, m. p. 192°, from chloroform–methanol. Continued crystallisation from chloroform gave (±)-*isorotenolone B* (2·33 g.), prisms, m. p. 242—243° (decomp.; pre-heated Kofler hot-stage) (Found: C, 67·5; H, 5·4; active H, 0·25. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4; active H, 0·25%), $\lambda_{max.}$ (in $CHCl_3$) 246 (4·69), 248 (4·69), 262 (4·25), 283 (4·16), and 335 (3·70), $\lambda_{max.}$ (alkaline ethanol) 242 (4·69), 260 (4·18), 278 (4·03), and 330 (3·54) mμ. Methylation with methyl iodide and silver oxide gave a little dehydroisorotenone (m. p. and mixed m. p. 195°) together with (±)-*isorotenolone B methyl ether*, m. p. 166° (Found: C, 67·75; H, 5·8. $C_{24}H_{24}O_7$ requires C, 67·9; H, 5·7%). A second form, m. p. 145°, of the ether was also encountered.

The mother-liquors from the chloroform crystallisation were diluted with methanol and concentrated, to give crystals which when recrystallised from chloroform–methanol formed needles of (±)-isorotenolone A, m. p. 208—209° (8·8 g.) (Found: C, 67·3; H, 5·55; active H, 0·27%), $\lambda_{max.}$ (in $CHCl_3$) 246 (4·76), 252 (4·76), 264 (4·32), 285 (4·25), 297 (3·98), and 335 (3·72), $\lambda_{max.}$ (alkaline ethanol) 243 (4·84), 247 (4·82), 260 (4·39), 279 (4·21), and 332 (3·83) mμ. Methylation as above gave (±)-isorotenolone A methyl ether, m. p. 152°, together with a little dehydroisorotenone. Neither (±)-isorotenolone formed a toluene-*p*-sulphonyl derivative, or an acetyl derivative (with keten): both were recovered unchanged after 6 hours' refluxing with active manganese dioxide in acetone; both failed to react with iodine and sodium acetate in dioxan in 12 hr. at 20°. LaForge and Haller[1] give m. p. 203—204° (methyl ether, m. p. 153°) for (±)-isorotenolone I, and m. p. 193—194° (methyl ether, m. p. 133—134°) for (±)-isorotenolone II. The former is almost pure isorotenolone A, but the latter corresponds to our material of m. p. 192° (the infrared spectrum of the authentic sample kindly supplied by Dr. H. L. Haller was identical) and is a mixture of (±)-isorotenolone A and B, as was shown spectroscopically and by methylation. Isorotenolone II (0·7 g.), when methylated as above, gave, after chromatography on alumina (N3) from benzene, (±)-isorotenolone A and B methyl ethers, m. p. and mixed m. p. 152—153° and 144—145° (second form), respectively; a little dehydroisorotenone was also formed.

(±)-*Isorotenolones by Treatment of* 6a,12a-*Dehydroisorotenol Acetate* (IVc) *with t-Butyl Hydroperoxide.*—The acetate (150 mg.) in benzene (0·5 ml.) was treated with t-butyl hydroperoxide (0·5 ml.) and Triton-B reagent (0·25 ml.). After 12 hr. more hydroperoxide (0·5 ml.) was added. After a further 3 hr. the mixture was washed with brine and chromatographed from benzene–chloroform (1 : 1) on alumina (K1), to give a mixture of (±)isorotenolones A and B, m. p. 187—190° not depressed on admixture with " isorotenolone II; " the infrared curves (mull) were almost superimposable.

Oxidation of (±)- *and* (−)-*Isorotenone with Dichromate in Acetic Acid.*—(−)-6aβ,12aβ-Isorotenone (7 g.) in acetic acid (175 ml.) was added to a warm solution of sodium dichromate (3·5 g.) in acetic acid (35 ml.) and kept for 12 hr. The product was poured into water and chromatographed from benzene–light petroleum (b. p. 60—80°) (1 : 1) on alumina (A5). The gum was treated with methanol. The insoluble solid, crystallised from chloroform–benzene, gave 6aβ,12aα-*isorotenolone B* (XIc) (50 mg.), plates, m. p. 220° (decomp.; br.), $[\alpha]_D^{19}$ +366° (*c* 1·5 in $CHCl_3$) (Found: C, 67·1; H, 5·6%; *M*, 416. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%; *M*, 410). The infrared spectrum (chloroform) was identical with that of (±)-isorotenolone B.

Concentration of the methanol solution and crystallisation at 0° gave 6aβ,12aβ-*isorotenolone A* (IXc) as the methanol solvate (4·2 g.), m. p. 96—97° (decomp.), $[\alpha]_D^{25}$ −83·5° (*c* 2 in C_6H_6), $[\alpha]_D^{16}$ −52° (*c* 2 in $CHCl_3$) (Found: C, 64·9, 65·2; H, 6·0, 5·9; OMe, 20·5. $C_{23}H_{22}O_7$, $CH_3{\cdot}OH$ requires C, 65·15; H, 5·9; OMe, 21·05%), $\lambda_{max.}$ (in $CHCl_3$) 246, 252, 264, 285, 298, and 336 mμ. In the infrared (CaF_2, CCl_4; $< \sim 0{\cdot}005$M) there were bands at 3645 (free primary OH of methanol) and 3503 cm.$^{-1}$ (intramolecularly bonded hydroxyl) and also (NaCl,$CHCl_3$) 1675 (aryl conj. ketone), 1613, 1595, and 1502 (aryl) cm.$^{-1}$. When heated *in vacuo* at 105—110° the substance frothed slowly and the glass did not crystallise again although its infrared spectrum in chloroform was the same as that of (±)-isorotenolone A. The solvate was heated at 120° and the distillate identified as methanol (α-naphthylurethane, m. p. and mixed m. p. 123°).

XUM

(±)-Isorotenone (500 mg.) was treated with potassium dichromate (200 mg.) in warm acetic acid (20 ml.) and kept overnight. Working up as above gave, after chromatography from benzene–chloroform (3 : 1) on alumina (A3) and crystallisation from chloroform–methanol, (±)-isorotenolone A, m. p. and mixed m. p. 208—209°.

Oxidation of (+)-Isorotenone with Dichromate in Acetic Acid.—(+)-6aα,12aα-Isorotenone [3] (10 g.) {m. p. 183—184°, $[\alpha]_D^{18}$ +82° (*c* 2 in C_6H_6)} in glacial acetic acid (200 ml.) was treated with potassium dichromate (6 g.) in water (20 ml.) at 60° for 30 min. After being kept overnight the mixture was worked up as above and chromatographed from benzene on alumina (N3). The resulting glass was dissolved in methanol, and (±)-isorotenolone A (730 mg.), m. p. and mixed m. p. 209—210°, crystallised and was removed. (+)-6aα,12aα-*Isorotenolone A* (Xc) crystallised as the methanol solvate (4·7 g.), m. p. 96° (decomp.) (Found: C, 65·6; H, 5·7%), $[\alpha]_D^{19}$ +81° (*c* 2 in C_6H_6), $[\alpha]_D^{16}$ +53° (*c* 2 in $CHCl_3$). When (+)- and (−)-isorotenolone A methanol solvates (100 mg.) were crystallised together from chloroform–methanol, (±)-isorotenolone A (unsolvated; 186 mg.) was isolated, with m. p. and mixed m. p. 209—210°.

(±)-*Isorotenolone A Acetate.*—(*a*) Isorotenone (2 g.) in glacial acetic acid (80 ml.) was shaken at 20° for 48 hr. with glacial acetic acid (100 ml.) saturated with lead tetra-acetate. The product was poured into water (1 l.), and the solid was filtered off and warmed with methanol. Crystallisation of the insoluble material (from chloroform–methanol) gave isorotenonone (76 mg.), m. p. and mixed m. p. 251°, $\lambda_{max.}$ (in $CHCl_3$) 295 (4·36), 274 (4·40), 261 (4·38), and 403 (3·88) mμ, $\nu_{max.}$ 1733 (unsaturated lactone), 1650 (C=O), 1613, 1587, 1563, and 1527 (aryl) cm.$^{-1}$. The methanolic solution crystallised, to give (±)-*isorotenolone A acetate* (920 mg.), m. p. and mixed m. p. 165° (Found: C, 66·6; H, 5·35%; *M*, 447. $C_{25}H_{24}O_8$ requires C, 66·4; H, 5·3%; *M*, 452). A second form, diamonds, m. p. 179°, was also encountered: its solution spectrum is identical with that of the form, m. p. 165°.

(*b*) Iodine (8 g.) in ethanol (100 ml.) was added to (−)-isorotenone (12 g.) in ethanol (300 ml.) containing sodium acetate (30 g.) and kept at 60°. The solution was partly evaporated, allowed to crystallise, and filtered, to give 6a,12a-dehydroisorotenone (6 g.), m. p. and mixed m. p. 196° (decomp.). The filtrate was poured into water, and the precipitated solid was dried and chromatographed from benzene–chloroform (3 : 1) on alumina (N1), to give more dehydroisorotenone, (±)-isorotenone, and (±)-isorotenolone A acetate (340 mg.), m. p. and mixed m. p. 165°. [For the direct acetylation of (±)-isorotenolone A and B see elsewhere.[2]]

(±)-Isorotenolone A acetate (1 g.) was treated with ethanolic 10% sodium hydroxide (50 ml.) at 40° for 2 hr., then poured into water, and the suspension was extracted with chloroform. The extract was dried and evaporated. The residue was chromatographed from benzene–chloroform (3 : 1) on alumina (N3), to give (±)-isorotenolone A (116 mg.), needles (from chloroform–methanol), m. p. and mixed m. p. 206—207°, and (±)-isorotenolone B (27 mg.), m. p. 239° (decomp.) (from the same solvents): the infrared spectrum of the latter was identical with that of an authentic specimen.

Acid-catalysed Dehydration of the Isorotenolones.—(*a*) (±)-Isorotenolone A (50 mg.) was refluxed for 15 min. with 10% sulphuric acid in methanol (5 ml.). After cooling, recrystallisation of the crystals from chloroform–methanol gave 6a,12a-dehydroisorotenone (39 mg.), m. p. and mixed m. p. 195° (decomp.). Similarly (±)-isorotenolone B (50 mg.), (+)-isorotenolone B (5 mg.), and (−)-isorotenolone A (10 mg.) gave dehydroisorotenone (41, 4, and 6 mg., respectively). (*b*) The isorotenolone (*ca.* 10 mg.) was dissolved in a 10% solution of sulphuric acid in tetrahydrofuran, with shaking for the first 5 min. Light absorption readings at 316 mμ were then taken with the following results (density increments in parentheses): (±)-isorotenolone A (10·77 mg.: initial dens. 0·392), 20 (0·014), 30 (0·019), 40 (0·024), 60 (0·032), 90 (0·039), 120 (0·042), 180 (0·046) min.; (±)-isorotenolone B (10·57 mg.: initial dens. 0·380), 10 (0·032), 20 (0·043), 50 (0·058), 70 (0·062), 95 (0·067), 115 (0·070), 140 (0·078), 170 (0·087), 195 (0·092) min. The absorption at 316 mμ (ε 2300) of a 10% solution of dehydroisorotenone in tetrahydrofuran was stable; so was that of (±)-isorotenolone A (ε 400) and B (ε 370) at 316 mμ in tetrahydrofuran.

Degradation of (±)-Isorotenolone A and B with Zinc Dust and Alkali.—(±)-Isorotenolone A (1 g.) was refluxed and stirred with zinc dust (2·5 g.), 15% aqueous potassium hydroxide (15 ml.), and ethanol (35 ml.) for 3 hr. The mixture was cooled, filtered, acidified, and evaporated, and the residue was extracted with ether. The ethereal extracts were themselves extracted with 2% aqueous potassium hydroxide. The residual ethereal solution was evaporated, to give isorotenol (135 mg.), plates (from methanol), m. p. 131°, $\lambda_{max.}$ (in acid

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ethanol), 243 (4·58), 250 (4·56), 263 (4·05), 284 (4·05), and 338 (3·46) mμ, $\nu_{max.}$ 1631 (chelated C=O), 1621, 1597, and 1499 (aryl) cm.$^{-1}$; the chelated-hydroxyl absorption is a broad band emerging from both sides of the C–H stretching complex. The alkaline extracts were acidified, to give isoderritol, yellow needles (314 mg.) (from methanol), m. p. 148°, $\lambda_{max.}$ (in $CHCl_3$), 242 (4·53), 252 (4·46), 291 (4·32) and 368 (4·00) mμ, $\nu_{max.}$ 1631 (chelated C=O), 1605, 1582, and 1497 (aryl) cm.$^{-1}$ (chelated hydroxyl as above plus intermolecularly bonded hydroxyl 3330 cm.$^{-1}$). Under the same conditions (±)-isorotenolone B (1 g.) gave isorotenol (58 mg.), m. p. 131° and isoderritol (160 mg.), m. p. 148°.

Pressure Hydrogenation of (±)-*Isorotenolone A and B.*—(±)-Isorotenolone A (1 g.) was hydrogenated in ethyl acetate (25 ml.) over Adams platinum catalyst (200 mg.) at 95°/50 atm. for 6 days. Working up gave a gum which on chromatography from benzene on alumina (A3) gave the *deoxy-compound* (Vb; but without stereochemical implications) (29 mg.), m. p. 160° (Found: C, 72·25, 72·2; H, 6·9, 7·05. $C_{23}H_{26}O_5$ requires C, 72·25; H, 6·85%), $\nu_{max.}$ 1621, 1610, and 1495 (aryl) cm.$^{-1}$. The infrared spectrum (chloroform) was very closely similar to that of (Vb; 6aβ,12aβ,5′β), m. p. 172°. It may be the same as the product, m. p. 160°, obtained when 6a,12a-dehydroisorotenone was catalytically hydrogenated.[17] Similarly hydrogenated, (±)-isorotenolone B gave the *deoxy-compound* (Vc) (27 mg.), m. p. 149° (from ethanol), in which ring E has not been reduced (Found: C, 72·7; H, 6·4. $C_{23}H_{24}O_5$ requires C, 72·6; H, 6·35%), $\nu_{max.}$ 1621, 1592, and 1497 cm.$^{-1}$.

(±)-*Tephrosin and* (±)-*Isotephrosin.*—(±)-Deguelin (200 mg.) in ethanol (20 ml.) and N-sodium hydroxide (1 ml.) was aerated for 24 hr. After 12 hr. at 0° crystals (150 mg.), m. p. 192—195°, had been deposited; they were chromatographed from benzene–chloroform (1 : 1) on alumina (K1), to give (±)-isotephrosin (14 mg.), prisms, m. p. 253—254° (lit.,[8b,18] m. p. 252°, 260°), and then (±)-tephrosin (82 mg.), plates (from methanol), m. p. 201°. An authentic specimen of the latter from natural sources had m. p. 197° (mixed m. p. 198—199°; lit.,[8a,18] m. p. 197°, 201°). (±)-Tephrosin had $\lambda_{max.}$ 238 (4·36), 251 (4·37), 271 (4·47), 300 (4·02), and 317 (3·97) mμ.

Dehydration of (±)-*Tephrosin.*—(*a*) (±)-Tephrosin (100 mg.) was refluxed with a 10% solution (3 ml.) of sulphuric acid in methanol for 30 min. The crystals which separated recrystallised from chloroform–methanol, to give 6a,12a-dehydrodeguelin (64 mg.), pale yellow rods, m. p. 230—231°, $\lambda_{max.}$ 220, 236, 259, 278, and 314 mμ. (*b*) (±)-Tephrosin (100 mg.) was warmed at 60—65° for 20 min. with sulphuric acid (0·5 ml.) in glacial acetic acid (1 ml.). The product was chromatographed from benzene–chloroform (1 : 1) on alumina (A1), to give 6a,12a-dehydrodeguelin, m. p. and mixed m. p. 228—229°. (*c*) (±)-Tephrosin (100 mg.) was heated under reflux with sodium acetate (100 mg.) in acetic anhydride (1 ml.) for 2 hr. Methanol was added and the solid which separated was chromatographed as above, to give 6a,12a-dehydrodeguelin, m. p. and mixed m. p. 231°. These three specimens had identical ultraviolet and infrared properties [$\nu_{max.}$ 1637 (C=O), 1621, 1603, 1572, 1502 (aryl) cm.$^{-1}$]. This agrees with the view of Boam and his co-workers [8d] on earlier claims.[19]

Reduction of (±)-*Isorotenolone A with Borohydride.*—(±)-Isorotenolone A (1 g.) in tetrahydrofuran–water (1 : 1; 50 ml.) was kept with potassium borohydride (3 g.) at 0° for 36 hr. The mixture was refluxed for 1 hr., 20% aqueous potassium carbonate (20 ml.) was added, and refluxing was continued for 3 hr. The product was poured on ice and filtered off (970 mg.; m. p. 206°). Crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave the (±)-*A diol* (XIX—XXc), m. p. 218° (632 mg.) (Found: C, 67·3; H, 5·9. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·85%), $\lambda_{max.}$ (in $CHCl_3$) 253 (4·24), 260 (4·24), 281i (3·83), 291 (3·97), and 299 (3·78) mμ, $\nu_{max.}$ (mull) 3483 (OH), 1618, 1605, 1590, and 1508 (aryl) cm.$^{-1}$. Another preparation was worked up chromatographically but a second diol was not found. When shaken with activated manganese dioxide in acetone for 48 hr. the (±)-A diol was reconverted into (±)-isorotenolone A. Reduction of (±)-isorotenolone A (2·7 g.) with sodium borohydride (2·7 g.) gave the (±)-A-diol (2·17 g.), plates, m. p. 216—218° (decomp.). The diol was unchanged after 48 hours' refluxing with sodium ethoxide in ethanol.

Reduction of (±)-*Isorotenolone B with Borohydride.*—(±)-Isorotenolone B (1 g.) in tetrahydrofuran (50 ml.) and ethanol (100 ml.) was kept with sodium borohydride (1 g.) at 50° for 30 min. The mixture was cooled, then set aside for 12 hr., and acetone (25 ml.) was added.

[17] Butenandt and Hildebrandt, *Annalen*, 1930, **477**, 245.
[18] Clark, *J. Amer. Chem. Soc.*, 1943, **65**, 27.
[19] Merz and Schmidt, *Arch. Pharm.*, 1935, **273**, 1.

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After evaporation, the residue was extracted with chloroform, and the extract was washed with 2N-hydrochloric acid and water and dried. Evaporation and crystallisation from chloroform–methanol gave the (±)-*B_1 diol* (XXIII—XXIVc) (405 mg.), plates m. p. 251—252° (decomp.; pre-heated block at 220°) or 263° (decomp.; preheated block at 250°) (Found: C, 67·2; H, 5·8. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·85%), $\lambda_{max.}$ (in $CHCl_3$) 253 (4·28), 258 (4·28), 280i (3·88), 290 (3·95), and 296i (3·85) mμ, $\nu_{max.}$ (mull) 3425i, 3356 (OH), 1610, 1600, 1582, and 1511 (aryl) cm.$^{-1}$. The chloroform mother-liquors were concentrated, methanol was added, and the concentration was repeated. This was done several times and the methanol solution was then set aside for 2 days. After filtration from a small amount of crystalline material, the solution was evaporated. The glassy product, crystallised from benzene–cyclohexane, gave the (±)-*B_2 diol* (XXV—XXVIc) (216 mg.), prisms, m. p. 213° (decomp.; br.) (Found: C, 66·85; H, 6·0%), $\nu_{max.}$ (mull) 3497, 3333 (OH), 1623i, 1613, 1600, 1587, and 1505 (aryl) cm.$^{-1}$. The mull spectra of (±)-A, (±)-B_1, and (±)-B_2 diols, although having a general similarity, are distinguishable from each other. When shaken with active manganese dioxide (1·5 g.) in acetone for 48 hr. the (±)-B_1 diol (152 mg.) gave (±)-isorotenolone B (143 mg.). The (±)-B_2 diol (50 mg.) was resistant to oxidation at 20° but, when refluxed in acetone with active manganese dioxide (1 g.) for 24 hr., gave (±)-isorotenolone B (18 mg.).

Reduction of (+)- *and* (−)-*Isorotenolone A with Borohydride.*—(−)-6aβ,12aβ-Isorotenolone A (methanol solvate; 1·5 g.) in ethanol (30 ml.) was reduced with sodium borohydride. Chromatography from chloroform on alumina (K3) gave the (−)-6aβ,12aβ,12α-*diol* (XIXc) (1·19 g.), m. p. 175—177° [from chloroform–light petroleum (b. p. 60—80°)], $[\alpha]_D^{20}$ −157° (*c* 2 in $CHCl_3$) (Found: C, 66·8; H, 5·7. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·85%). (+)-6aα,12aα-Isorotenolone A (methanol solvate; 1·5 g.) similarly gave the (+)-6aα,12aα,12β-*diol* (XXc) (1·24 g.), m. p. 175—176°, $[\alpha]_D^{20}$ +160° (*c* 2 in $CHCl_3$) (Found: C, 66·7; H, 5·95%). Each diol was oxidised back to its ketol precursor, m. p. and mixed m. p. 97—98°, when shaken for 1 hr. with active manganese dioxide in acetone. The diols, crystallised together from chloroform, gave the (±)-A-diol, m. p. and mixed m. p. 216° (decomp.). The infrared solution spectra of the (±)-, (+)-, and (−)-A-diols are identical. Those of the (+)- and (−)-diols as mulls (identical) show only minor differences from the mull spectrum of the (±)-compound.

Catalytic Hydrogenation of (±)-*Isorotenolone A and B.*—(*a*) (±)-Isorotenolone A (1 g.) in glacial acetic acid (50 ml.) was hydrogenated over Adams platinum catalyst (250 mg.) at atmospheric pressure for 6 hr. The mixture was filtered into water, and the precipitated solid was crystallised from ethyl acetate–light petroleum (b. p. 60—80°), to give the (±)-A-diol (657 mg.), m. p. and mixed m. p. 216—217° (infrared confirmation). (*b*) (±)-Isorotenolone B (1 g.) in ethyl acetate (25 ml.) was hydrogenated over Adams catalyst (200 mg.) at 60°/80 atm. for 2 days. Working up and crystallisation from ethyl acetate–ethanol gave the (±)-B_1-diol (452 mg.), needles, m. p. 263—264° (decomp.; br): identity was established by comparison of mull spectra.

Treatment of the (±)A- *and* (±)B_1-*Diols with Acid.*—(*a*) The (±)-A-diol (100 mg.) was refluxed with 10% methanolic sulphuric acid (5 ml.) for 1 hr. and the product was poured into water and extracted with chloroform. The extract yielded (±)-isorotenone (33 mg.), needles (from methanol), m. p. and mixed m. p. 171°. The mother-liquors gave no precipitate with Brady's reagent. (*b*) The (±)-B_1-diol (200 mg.) similarly gave a product (no precipitate with Brady's reagent) which after chromatography from benzene–chloroform (3 : 1) on alumina (N1) gave (±)-isorotenone (26 mg.), m. p. and mixed m. p. 171°. A second experiment worked up as in (*a*) gave (±)-isorotenone (44 mg.) from (±)-B_1-diol (100 mg.).

The (±)-6,6a-*Dihydrorotoxen Derivative* (XXVII—XXVIIIc).—The 12β-hydroxy-compound, m. p. 193° (4 g.), made by reducing (±)-isorotenone with borohydride,[2] was treated with phosphorus oxychloride (12 ml.) in dry pyridine (30 ml.) at 80° for 90 min. The mixture was poured into water and extracted with chloroform. After being washed with 4N-hydrochloric acid and water the extract was dried and evaporated, and the residue was chromatographed from benzene–chloroform (3 : 1) on alumina (A1) and crystallised from chloroform–methanol, to give the (±)-6,6a-*dihydrorotoxen derivative* (XXVII—XXVIIIc) (2·13 g.), plates, m. p. 180° (Found: C, 72·75; H, 5·8. $C_{23}H_{22}O_5$ requires C, 73·0; H, 5·85%), $\lambda_{max.}$ 255 (4·50), 267 (4·48), 277 (4·49), 312 (3·93), 338i (4·29), 357 (4·49), and 376 (4·40) mμ, $\nu_{max.}$ 1623, 1595, and 1502 (aryl and C=C) cm.$^{-1}$.

Isorotenone Enol-acetate.—This *acetate* was prepared by the sodium acetate–acetic anhydride technique for the purposes of ultraviolet comparison; it had m. p. 134° (Found: C, 68·5; H,

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5·5. $C_{25}H_{24}O_7$ requires C, 68·8; H, 5·55%), $\lambda_{max.}$ 255 (4·49), 265 (4·38), 274 (4·30), 312 (3·85), 333i (4·11), 352 (4·31), and 370 (4·24) mμ, $\nu_{max.}$ 1763 cm.$^{-1}$ (Ac).

Treatment of the (±)-6,6a-*Dihydrorotoxen Derivative* (XXVII—XXVIIIc) *with Osmium Tetroxide.*—The (±)-6,6a-dihydrorotoxen (600 mg.) and osmium tetroxide (500 mg.) in dry dioxan (20 ml.) and pyridine (2 drops) were kept in the dark for 20 days. The osmium complex was decomposed by passage of hydrogen sulphide (12 hr.), the osmium sulphide was filtered off, and the filtrate was poured into water. After 12 hr. the product was filtered off and crystallised from ethyl acetate, to give the (±)-B_1-diol (272 mg.) having an infrared spectrum (mull) identical with that of the authentic specimen above. Oxidation with active manganese dioxide gave isorotenolone B, m. p. and mixed m. p. 241° (decomp.) (infrared confirmation). Addition of light petroleum to the ethyl acetate mother-liquors gave unchanged 6,6a-dihydrorotoxen precursor (78 mg.).

Oxidation of the Isorotenolols with Lead Tetra-acetate.—The diol (20 mg.) and 0·1N-lead tetra-acetate in acetic acid (2 ml.) were rapidly and accurately made up to 10 ml. with acetic acid. At intervals 1 ml. portions were removed and titrated against 0·1N-sodium thiosulphate. The (±)-B_1-diol had completely reacted before a reading at 2 min. The $t_{1/2}$ and $t_{3/4}$ for the (±)-B_2-diol were 8½ and 16 min., respectively; for the (±)-A diol they were 2 and 3½ min., respectively.

Oxidation of the Isorotenolols with Periodic Acid.—Periodic acid (1 g.) in 50% aqueous solution was diluted with methanol (5 ml.) and added to the (±)-A-diol (XIX—XXc) (250 mg.) in dioxan (25 ml.). The mixture was shaken for 24 hr. and poured into water (100 ml.). The precipitate was filtered off and crystallised from acetone–methanol, to give the (±)-*keto-aldehyde* (XXIX—XXXc) (228 mg.), needles, m. p. 182° (Found: C, 67·05; H, 5·4. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%), $\lambda_{max.}$ (CaF_2, $CHCl_3$) 1675 cm.$^{-1}$ (ketone and aldehyde not resolved). The (±)-B_1-diol (250 mg.) gave an identical keto-aldehyde (172 mg.), m. p. and mixed m. p. 182°. The (±)-B_2-diol (50 mg.) gave the same keto-aldehyde (19 mg.), m. p. 179—180°, mixed m. p. 180—181°. The infrared spectra (mulls) of the three specimens were the same.

The (−)-6aβ,12aβ,12α-diol (XIXc) (250 mg.) gave the 6aβ-*keto-aldehyde* (XXIXc) (172 mg.), needles (from acetone–methanol), m. p. 189—190° (Found: C, 66·5, 66·5; H, 5·2, 5·4. $C_{23}H_{22}O_7,\frac{1}{2}CH_3{\cdot}OH$ requires C, 66·25; H, 5·65%), $[\alpha]_D^{21}$ +205° (*c* 2 in $CHCl_3$). The (+)-6aα,12aα,12β-diol (XXc) (250 mg.) gave the 6aα-*keto-aldehyde* (XXXc) (165 mg.), m. p. 190° (from the same solvent mixture) (Found: C, 66·5, 66·6; H, 5·35, 5·7%), $[\alpha]_D^{21}$ −202° (*c* 2 in $CHCl_3$). Crystallised together the enantiomorphs gave the (±)-keto-aldehyde, m. p. and mixed m. p. 182°. The chloroform infrared spectra of the three keto-aldehydes were identical except for a band due to methanol in the solvates.

Reduction of (±)-*Isorotenolone B Methyl Ether with Sodium Borohydride.*—The ether (1·5 g.; m. p. 145°) in ethanol (150 ml.) was reduced with sodium borohydride (1·5 g.) in the usual way and gave the (±)-12a-*monomethyl ether* of isorotenolol B (XXIII—XXIVc) (1·42 g.) (Found: C, 67·55; H, 6·25. $C_{24}H_{26}O_7$ requires C, 67·6; H, 6·15%), m. p. 262° (decomp.; br). The ether could be chromatographed on alumina (K1) but in one experiment in which chromatography on " acid " alumina was employed the 12a-ether and (±)-isorotenone were found. Refluxing the ether (100 mg.) with 5% hydrochloric acid in dioxan gave (±)-isorotenone (64 mg.), m. p. and mixed m. p. 171°.

The stereochemistry of the 12a-monomethyl ether was decided by methylation to the dimethyl ether, m. p. 172° (decomp.) (from pentane), identical (mixed m. p.) with the dimethyl ether from (±)-isorotenolol B_1, m. p. 170°, and different from (±)-isorotenolol B_2 dimethyl ether, m. p. 89° (decomp.).

(±)-*Isorotenolone C.*—(−)-Isorotenone (10 g.) in 5% methanolic potassium hydroxide (130 ml.) was warmed to 60° and 30% hydrogen peroxide (14 ml.) was added in portions. Heating was continued for 30 min. and the whole was set aside for 12 hr. and then filtered, to give (±)-isorotenolone C (6·4 g.), m. p. 209° raised to 211—212° (plates) after crystallisation from chloroform–methanol. It did not depress the m. p. of LaForge and Haller's original specimen [1] m. p. 210—212° (we thank Dr. Haller for this). (±)-Isorotenolone C (Found: C, 67·15; H, 5·6. Calc. for $C_{23}H_{22}O_7$: C, 67·3; H, 5·4%) had $[\alpha]_D^{20}$ 0°, $\lambda_{max.}$ (in $CHCl_3$) 241 (4·76), 247i (4·69), 264i (4·07), 281 (4·11), 292i (3·98), and 335 (3·74) mμ, $\lambda_{max.}$ (in alkaline ethanol) 239 (4·72), 245 (4·64), 259i (4·02), 281 (4·02), 290i (3·95), and 333 (3·70) mμ (the curve in acid ethanol was very similar), $\nu_{max.}$ ($CHCl_3$) 1706, $\nu_{max.}$ (mull) 1684 (C=O) cm.$^{-1}$. On methylation with methyl iodide–silver oxide the methyl ether was obtained, having m. p. 157°, $\lambda_{max.}$ 240 (4·69), 246 (4·62), 278

(4·06), 282 (4·07), and 333 (3·73) mμ, $\nu_{max.}$ (in $CHCl_3$) 1706 (C=O), 1629, 1597, and 1504 (aryl) $cm.^{-1}$, $\nu_{max.}$ (mull) 1706 (C=O), 1623, 1585, and 1506 (aryl) $cm.^{-1}$ (lit.,[1] m. p. 160°). Refluxing sodium acetate and acetic anhydride or keten gave the monoacetate, m. p. 142—143°, $\nu_{max.}$ 1742 (OAc), 1704 (C=O), 1626, 1592, and 1502 (aryl) $cm.^{-1}$ (lit.,[1] m. p. 145°). By heating the alcohol with toluene-*p*-sulphonyl chloride in pyridine the *toluene*-p-*sulphonate* was obtained as prisms [from benzene–light petroleum (b. p. 60—80°)], m. p. 187° (Found: C, 63·65; H, 5·1. $C_{30}H_{28}O_9S$ requires C, 63·9; H, 5·0%), $\nu_{max.}$ 1706 (C=O) $cm.^{-1}$. The derivative was recovered in poor yield after treatment with sodium n-butoxide in butan-1-ol.

(±)-Isorotenolone C was unaffected by refluxing 10% ethanolic potassium hydroxide or 1 : 2 sulphuric–acetic acid. It gave no ferric chloride colour. When dissolved in concentrated sulphuric acid and poured into water it gave a deep green precipitate, soluble in methanol to a deep blue solution; adding ethanolic sodium hydroxide discharged the blue colour. (±)-Isorotenolone C was unchanged after attempted hydrogenation over Adams platinum at 95°/55 atm. for 12 hr. The substance was not oxidised by lead tetra-acetate, sodium bismuthate, chromium trioxide–pyridine, or chromium trioxide in concentrated sulphuric acid and acetone at 20°. More severe oxidative conditions gave no identifiable product. (±)-Isorotenolone C was not affected by iodination in dioxan at 20° (24 hr.), by refluxing it with an acetone suspension of manganese dioxide, or by keeping it with ethereal diazomethane at 0° for 60 days.

In one preparation (±)-isorotenolone C, m. p. 189—190°, was isolated. One crystallisation from chloroform–methanol raised the m. p. to 209—210°. The two forms had identical infrared solution spectra and nearly identical mull spectra. LaForge and Haller [1] give m. p. 188—189° for isorotenolone D. If the temperature in the preparation is not sufficiently high, isorotenolones A and B can be isolated.

6′,7′-Dihydrorotenolone C.—Dihydrorotenone (2 g.) was treated with 30% hydrogen peroxide (5 ml.) in 5% methanolic potassium hydroxide, as above. After being kept at 0°, the mixture was poured into water; extraction with ether gave a glass which was extracted with hot light petroleum (b. p. 100—120°). The petroleum extracts were kept at 0°; after 3 months *6′,7′-dihydrorotenolone C* crystallised; it had m. p. 187° (800 mg.) (Found: C, 66·75; H, 6·0. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·85%), $[\alpha]_D^{18}$ −79° (*c* 0·9 in $CHCl_3$), $\nu_{max.}$ (in $CHCl_3$) 3586, 3381 (OH), 1698 (C=O), 1621, 1600, and 1486 (aryl) $cm.^{-1}$, $\nu_{max.}$ (mull) 1692 (C=O) $cm.^{-1}$.

Degradation [1] of (±)-Isorotenolone C to Isorotenol (VIc) *and Isoderritol* (VIIc).—Isorotenolone C (2 g.) was treated under reflux for 3½ hr. with 15% aqueous potassium hydroxide (30 ml.), ethanol (70 ml.), and zinc dust (5 g.). Working up gave isorotenol [3] (0·26 g.), m. p. 132°, and isoderritol (0·72 g.), m. p. 148°, both identical with authentic specimens.

The Chloro-derivative of (±)-Isorotenolone C.—(±)-Isorotenolone C (1 g.) was refluxed with dry γ-collidine (15 ml.) and phosphorus oxychloride (4 ml.) for 2 hr. The mixture was poured on ice and extracted with chloroform. The extract was washed with 4N-hydrochloric acid and water, dried, and evaporated. Chromatography of the residual gum from benzene–chloroform (3 : 1) on alumina (A1) and crystallisation from light petroleum (b. p. 60—80°) gave the *monochloro-derivative* (XXXIV; R = Cl), m. p. 171°, $\nu_{max.}$ (in $CHCl_3$), 1711 (C=O), 1629, 1593, and 1505 (aryl) $cm.^{-1}$, $\nu_{max.}$ (mull) 1708 $cm.^{-1}$ (Found: C, 64·45; H, 5·0; Cl, 8·15. $C_{23}H_{21}ClO_6$ requires C, 64·4; H, 4·95; Cl, 8·25%).

Reduction of (±)-Isorotenolone C with Borohydride.—(±)-Isorotenolone C (1 g.) and potassium borohydride (3 g.) in tetrahydrofuran–ethanol (1 : 1; 75 ml.) were kept at 0° for 6 days. The solution was refluxed for 2 hr. and then refluxed overnight with 20% aqueous potassium carbonate (10 ml.). Working up gave the *diol* (840 mg.), plates [from ethyl acetate–light petroleum (b. p. 60—80°)], m. p. 197—198° (Found: C, 67·2; H, 6·0. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·85%), $\lambda_{max.}$ (in $CHCl_3$) 252 (4·29), 259 (4·27), 289 (4·06), and 295 (4·09) mμ, $\nu_{max.}$ (CaF_2, CCl_4; < ~0·005M) 3606 and 3574 $cm.^{-1}$, $\nu_{max.}$ (NaCl, $CHCl_3$), 3616, 3390 (OH), 1634i, 1621, 1590, and 1504 $cm.^{-1}$. When the diol was shaken with active manganese dioxide in acetone at 20°, (±)-isorotenolone C was formed almost quantitatively.

Preparation of Rotenolones by Alkaline Oxygenation.—Natural rotenone (50 g.) was suspended in 95% ethanol (1·5 l.), aqueous N-potassium hydroxide (30 ml.) was added, and a rapid stream of air was passed through the mixture for 3 days. The rotenone first dissolved and a granular precipitate was then formed. The latter (6·1 g.) was filtered off and crystallised from chloroform–ethanol to give rotenonone (19 mg.), yellow plates, m. p. 295° (mixed m. p. 296—297°), and crystals (4·9 g.), m. p. 207—219° (decomp.). The latter were further crystallised

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from chloroform–ethanol, to give 6aβ,12aα,5′β-*rotenolone* (XIa) (1·8 g.), large plates, m. p. 249—251° (decomp.) (Found: C, 67·0; H, 5·3. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%), $[\alpha]_D^{20}$ +420° (*c* 2 in $CHCl_3$), $\nu_{max.}$ (CaF_2, CCl_4; < ~0·005M) 3603 cm.$^{-1}$ (there were signs of a very weak band at 3556 cm.$^{-1}$), $\nu_{max.}$ (NaCl, $CHCl_3$) 3584 (OH), 3344 (intermolecularly bonded OH), 1692 (C=O), 1616, and 1504 (aryl) cm.$^{-1}$. The mother-liquors from the crystallisation were diluted with methanol and evaporated several times *in vacuo*, the methanol being renewed each time. Finally the product was recrystallised from ethanol, to give 6aα,12aβ,5′β-*rotenolone* (XIIa) (104 mg.), needles, m. p. 211—212° (Found: C, 67·3; H, 5·15%), $[\alpha]_D^{19}$ −78° (*c* 2 in $CHCl_3$). The solution infrared spectra of the two diastereoisomers were virtually the same.

The original filtrate from the aeration was just acidified with acetic acid and poured into water. The precipitate was filtered off, dried, and treated with ether. There remained material which contains a new substance which will not be considered here: the ether solution was dried and on refrigeration gave crystals, m. p. 132—135°, which when crystallised from methanol gave a mixture of 6aβ,12aβ,5′β- and 6aα,12aα,5′β-rotenolones (16·1 g.), prisms, m. p. 139—140° (Found: C, 67·25; H, 5·3%), $[\alpha]_D^{15}$ −140° (*c* 2 in $CHCl_3$), $\nu_{max.}$ (CaF_2, CCl_4, < ~0·005M) 3509 cm.$^{-1}$, $\nu_{max.}$ (NaCl, $CHCl_3$) 3521 (intramolecularly bonded OH), 1672 (C=O), 1616, and 1504 (aryl) cm.$^{-1}$ [rotenone has $\nu_{max.}$ 1674 (C=O) cm.$^{-1}$].

Oxidation of Natural Rotenone with Dichromate in Acetic Acid.—Rotenone (10 g.) in acetic acid (250 ml.) was treated with potassium dichromate (7 g.) in glacial acetic acid (100 ml.) and water (10 ml.) and kept at 50° for 30 min. and then at 20° for 24 hr. Pouring the solution into water (1 l.) gave a precipitate that was chromatographed from benzene–chloroform (1 : 1) on alumina (K1), elution being with chloroform. In order of elution there were obtained: rotenone (29 mg.), m. p. and mixed m. p. 296°; dehydrorotenone (262 mg.), m. p. and mixed m. p. 216°; a mixed fraction separable by treatment with hot methanol into dehydrorotenone (38 mg.) and solvated 6aβ,12aβ,5′β-rotenolone (IXa) (24 mg.); and a glass. The glass gave solvated 6aβ,12aβ,5′β-*rotenolone* (IXa) (5·7 g.) as large prisms, m. p. 88°, when crystallised from methanol (Found: C, 65·1; H, 5·9. $C_{23}H_{22}O_7,CH_3{\cdot}OH$ requires C, 65·1; H, 5·9%), $[\alpha]_D^{16}$ −189° (*c* 2 in $CHCl_3$).

Oxidation of (" *d-epi* ") 6aα,12aα,5′β-*Rotenone Concentrate with Dichromate in Acetic Acid.*—6aα,12aα,5′β-Rotenone concentrate (12 g.; $[\alpha]_D$ +10°) in glacial acetic acid (250 ml.) was heated at 50°, as above, with potassium dichromate (8 g.) in water (25 ml.). Working up as above by chromatography gave creamy-white solid (2·65 g.) which did not crystallise. It was purified by precipitation from acetone with water, to give powdery 6aα,12aα,5′β-*rotenolone* (Xa) (Found: C, 67·2; H, 5·55. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%), $[\alpha]_D^{18}$ +26° (*c* 1 in $CHCl_3$). The solution infrared spectra of the 6aα,12aα,5′β- and the 6aβ,12aβ,5′β-diastereoisomer, and their mixture formed in the aeration experiment, were virtually identical and showed clear differences from the series with the *trans*-B/C ring junction.

Reduction of cis-B/C *Rotenolones with Borohydride.*—6aβ,12aβ,5′β-Rotenolone (IXa; methanol solvate) (2·6 g.), in ethanol (150 ml.), was kept at 50° with sodium borohydride (1·5 g.) for 30 min. and then at 20° for 12 hr. Acetone (20 ml.) was added and the solvents were evaporated. The residue was dissolved in chloroform and washed with water, 4N-hydrochloric acid, and aqueous potassium carbonate, and then dried. Evaporation gave solid (2·3 g.) which crystallised from carbon tetrachloride and then methanol to give 6aβ,12aβ,12α,5′β-*rotenolol* (XIXa) as the methanol solvate, prisms, m. p. 125—126° (decomp.) (Found: C, 64·8; H, 6·5. $C_{23}H_{24}O_7,CH_3{\cdot}OH$ requires C, 64·85; H, 6·35%), $[\alpha]_D^{20}$ −152° (*c* 2 in $CHCl_3$).

6aα,12aα,5′β-Rotenolone (Xa) (2 g.) in ethanol (50 ml.) was reduced with sodium borohydride as above, to give 6aα,12aα,12β,5′β-*rotenolol* (XXa) as the methanol solvate (1·3 g.), m. p. 185° (decomp.) (Found: C, 64·95; H, 5·75%), $[\alpha]_D^{20}$ +120° (*c* 1 in $CHCl_3$). The infrared solution spectrum was virtually identical with that of the 6aβ,12aβ,12α,5′β-diastereoisomer.

The mixture (3·5 g.), m. p. 139—140°, of 6aβ,12aβ,5′β- and 6aα,12aα,5′β-rotenolones obtained from the aerial oxidation experiment was reduced with sodium borohydride (0·5 g.). Crystallisations of the product from methanol and chloroform–methanol gave 6aβ,12aβ,12α,5′β-rotenolol (0·8 g.), m. p. 123—124°, $[\alpha]_D^{18}$ −153° (*c* 2 in $CHCl_3$), identical with the specimen above. The mother-liquors were worked up by crystallisation from carbon tetrachloride, to give material of m. p. 147—153° (after softening from 126°). Chromatography from carbon tetrachloride on alumina (K1), and elution with chloroform and then chloroform–acetone, gave impure 6aα,12aα,12β,5′β-rotenolol (127 mg.), m. p. 156—157°, $[\alpha]_D^{20}$ +88·5° (*c* 2 in $CHCl_3$), from

carbon tetrachloride (unsolvated, identified spectroscopically). In another experiment 6aβ,12aβ,12α,5′β-*rotenolol* was also obtained unsolvated by crystallisation from carbon tetrachloride, forming plates, m. p. 191° (Found: C, 67·2; H, 5·9. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·85%), $[\alpha]_D^{15}$ −150° (*c* 2 in $CHCl_3$). The crude reduction product of the diastereoisomeric mixture, if crystallised several times from carbon tetrachloride, gave plates, m. p. 194°, $[\alpha]_D^{18}$ −40·5°; one recrystallisation from methanol then gave the 6aβ,12aβ,5′β-rotenolol, m. p. 125° (with liberation of methanol), $[\alpha]_D^{18}$ −154°.

Reduction of trans-B/C *Rotenolones with Borohydride.*—6aβ,12aα,5′β-Rotenolone (2 g.) in tetrahydrofuran (100 ml.) and ethanol (150 ml.) was reduced, as above, with sodium borohydride (0·5 g.). Working up by crystallisation from chloroform and then methanol–chloroform gave the 6aβ,12aα,12α,5′β-*rotenolol* (XXIIIa) (800 mg.), plates, m. p. 257° (decomp.) (Found: C, 67·2; H, 6·15. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·85%), $[\alpha]_D^{17}$ +196° (*c* 0·25 in $CHCl_3$). More (240 mg.) was isolated from the mother-liquors which were then evaporated and dissolved in benzene. Crystals, m. p. 237° (decomp.) (65 mg.), separated and were rejected. The solution was concentrated and cyclohexane was added. 6aβ,12aα,12β,5′β-*Rotenolol* (XXVa) (570 mg.), m. p. 180° (Found: C, 66·7; H, 5·7%), $[\alpha]_D^{17}$ +228° (*c* 1 in $CHCl_3$), crystallised and was further crystallised from the same solvent mixture. The solution infrared spectra of the 6aβ,12aα,12β,5′β- and 6aβ,12aα,12α,5′β-rotenolol are different.

6aα,12aβ,5′β-Rotenolone (100 mg.) in ethanol (25 ml.) was reduced with sodium borohydride (100 mg.) as usual. The product, a glass, partly crystallised from methanol, to give 6aα,12aβ,12β,5′β-*rotenolol* (XXIVa) (23 mg.), plates, m. p. 259° (decomp.; bl. or br.), 251° (decomp.; tube) (Found: C, 67·15; H, 5·55%), $[\alpha]_D^{16}$ −15° (*c* 0·5 in $CHCl_3$). Concentration of the liquors gave more (13 mg.). Finally the liquors were evaporated and chromatographed from benzene–chloroform (3 : 7) on alumina (K1), to give 6aα,12aβ,12α,5′β-*rotenolol* (XXVIa) (17 mg.), m. p. 157° (br) (from chloroform–cyclohexane) (Found: C, 66·95; H, 5·8%), $[\alpha]_D^{16}$ −50° (*c* 0·5 in $CHCl_3$), and further (11 mg.) 6aα,12aβ,12β,5′β-rotenolol. The solution infrared spectra of 6aα,12aβ,12β,5′β- (XXIVa) and 6aα,12aβ,12α,5′β-rotenolol (XXVIa) were different, but the solution spectra of the 6aβ,12aα,12α,5′β- (XXIIIa) and the 6aα,12aβ,12β,5′β-diol (XXIVa) are virtually indistinguishable: this applies also to the 6aβ,12aα,12β,5′β- (XXVa) and 6aα,12aβ,12α,5′β-pair (XXVIa).

Oxidation of Rotenolols with Manganese Dioxide.—6aβ,12aβ,12α,5′β-Rotenolol (100 mg.) was shaken with active manganese dioxide (1 g.) in acetone for 12 hr. Filtration, evaporation, and crystallisation from methanol gave solvated 6aβ,12aβ,5′β-rotenolone (63 mg.), m. p. and mixed m. p. 88°, $[\alpha]_D^{19}$ −185° (*c* 2 in $CHCl_3$). 6aβ,12aα,12α,5′β-Rotenolol (25 mg.) similarly gave 6aβ,12aα,5′β-rotenolone (17 mg.), m. p. and mixed m. p. 245° (decomp.), $[\alpha]_D^{18}$ +430° (*c* 1 in $CHCl_3$). Under the above conditions, 6aβ,12aα,12β,5′β-rotenolol (17 mg.) was unaltered but, after refluxing (48 hr.) 6aβ,12aα,5′β-rotenolone (13 mg.), m. p. and mixed m. p. 245°, $[\alpha]_D^{17}$ +406° (*c* 0·5 in $CHCl_3$), was obtained.

Oxidation of Rotenolols with Lead Tetra-acetate.—By the method described above, the 6aβ,12aβ,12α,5′β- (XIXa) and the 6aα,12aα,12β,5′β-rotenolol (XXa) each had $t_{1/2}$ and $t_{3/4}$ 2 and 3¾ min. The 6aβ,12aα,12β,5′β- (XXVa) and 6aα,12aβ,12α,5′β-diol (XXVIa) had $t_{1/2}$ 5¾ and 6½ min., and $t_{3/4}$ 13 and 14 min., respectively. 6aβ,12aα,12α,5′β- (XXIIIa) and 6aα,12aβ,12β,5′β-Rotenolol (XXIVa) reacted completely in less than 2 min.

Oxidation of Rotenolols with Periodic Acid.—6aβ,12aβ,12α,5′β-Rotenolol (XIXa) (250 mg.) in dioxan (25 ml.) was added to periodic acid (1 g.) in 50% aqueous methanol (5 ml.). The mixture was shaken for 24 hr. and poured into water. Filtration gave the 6aβ,5′β-*keto-aldehyde* (XXIXa) (189 mg.), needles, m. p. 216° (from acetone–methanol) (Found: C, 67·35; H, 5·7. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%), $[\alpha]_D^{18}$ +141° (*c* 2 in $CHCl_3$). 6aβ,12aα,12α,5′β-Rotenolol (250 mg.) gave the same keto-aldehyde (174 mg.), m. p. and mixed m. p. 216° (infrared mull confirmation), $[\alpha]_D^{18}$ +142° (*c* 2 in $CHCl_3$). 6aβ,12aα,12β,5′β-Rotenolol also gave the keto-aldehyde, m. p. and mixed m. p. 213° (infrared mull comparison).

6aα,12aα,12β,5′β-Rotenolol (XXa) (200 mg.) under the same conditions gave the 6aα,5′β-*keto-aldehyde* (XXXa) (162 mg.), needles, m. p. 196—197° (decomp.) (from acetone–methanol) (Found: C, 67·1; H, 5·3%), $[\alpha]_D^{18}$ −245° (*c* 2 in $CHCl_3$). 6aα,12aβ,12β,5′β-Rotenolol (XXIVa) (10 mg.) gave the same keto-aldehyde (6 mg.), m. p. and mixed m. p. 196—197° (infrared mull comparison).

The 6aβ,5′β- and the 6aα,5′β-keto-aldehyde have readily distinguishable mull spectra, but in chloroform solution they are virtually identical.

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UNIVERSITY OF LONDON, KING'S COLLEGE,
STRAND, LONDON, W.C.2.
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
S. KENSINGTON, LONDON, S.W.7.

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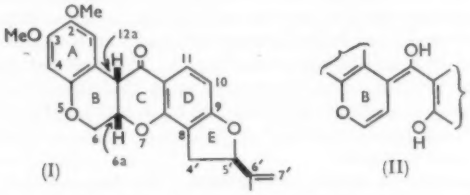
555. *Some Chemistry of the* B/C-*Ring System of Rotenoids.*

By L. CROMBIE, P. J. GODIN, D. A. WHITING, and K. S. SIDDALINGAIAH.

A scheme is drawn up to account for the behaviour of rotenone and rotenoids in basic media. Its validity is checked by isolation of various key substances. The chemical behaviour of the latter are studied and lend colour to the proposals. Certain chemical differences between the rotenone and the toxicarol series are explained by the influence of phenolic ionisation on the relative stability of two intermediates. Aspects of the chemistry of the B/C system are simultaneously examined.

THIS paper deals with certain aspects of the chemistry of the B/C ring system of rotenone (I) and its natural relatives, particularly the reactions in basic media. Such conditions cause racemisation of centres 6a and 12a, and Cahn and his colleagues [1] believed that an intermediate (IIa) * was implicated. Jennen,[2] extending views of Butenandt *et al.*,[3] preferred an intermediate (V). We consider Jennen's treatment of racemisation in the presence of weak bases to be essentially correct, but, with modifications, Cahn's intermediate is required to give a more complete picture of the effect of stronger bases on rotenone. In our view the annexed equilibria (III—X) are set up when the 6a proton is removed by a suitable base.



Although the 6′,7′-olefinic linkage in rotenone is readily shifted by acid treatment *via* carbonium ion intermediates to give the benzofuran isorotenone (IIIc) (centres 6a and 12a being in this case unaffected), in basic medium the configuration at 5′ is unaffected.[1] The ion (IVa) initially formed by action of a base can re-accept a proton giving back unchanged rotenone (IIIa) or rotenone with a *trans*-B/C fusion; the latter is thermodynamically disfavoured and has not yet been isolated. By electronic shifts as shown, ion (IVa) equilibrates with the intermediate ion (Va) which can re-cyclise to give (IIIa) or (VIIa). The equilibrium mixture of diastereoisomers (III—VIIa) is " mutarotenone;" in the case of isorotenone the product is the racemate (III—VIIc).[1] This equilibration is brought

* The lower case letter following the Roman numeral indicates that the complete structural series to which it belongs is as follows: a, 5′β-rotenone; b, 6′,7′-dihydro-5′β-rotenone; c, isorotenone; d, deguelin (R = H) or toxicarol (R = OH); e, 4′,5′-dihydrodeguelin (R = H) or 4′,5′-dihydrotoxicarol (R = OH); f, 6a,12a-dihydro-6*H*-rotoxen-12-one; g, dihydrorotenonic acid; h, rotenonic acid. The omitted pieces of the structures are given in full on p. 2846.

[1] Cahn, Phipers, and Boam, *J.*, 1938, 513.
[2] Jennen, *Bull. Soc. chim. belges*, 1952, **61**, 536.
[3] (*a*) Butenandt and McCartney, *Annalen*, 1932, **494**, 17; (*b*) Butenandt and Hilgetag, *ibid.*, 1933, **506**, 158.

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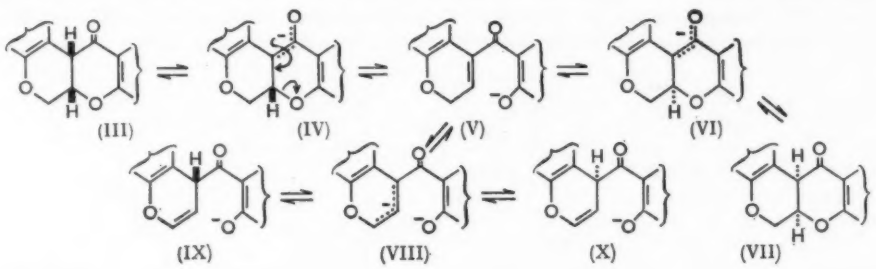
about by mild bases such as sodium acetate in ethanol, and the racemisation rate measures the formation of the ion (Vc). But in stronger bases the species (Vc) becomes involved in prototropic equilibration with the two diastereoisomers (IXa; 12aβ,5′β) and (Xa; 12aα,5′β) *via* the ion (VIII). Later in the paper the isolation of the pure key substances



(Va), (IXa), and (Xa) (protonated) is reported and their behaviour is examined; but, first, some points relating to mutarotenone will be cleared up.

Cahn and his colleagues view mutarotenone as a " quasi-racemic compound " but there is no evidence that it is other than a mixture of two diastereoisomers of rather similar properties. Its special status seems to have arisen from the unsuitability of benzene and ether–benzene as solvents for fractional crystallisation of the mixture. About 50% of natural rotenone can be separated from mutarotenone by using its ability to form a carbon tetrachloride solvate, but preparations of the 6aα,12aα,5′β-component (epirotenone) have hitherto been amorphous.[1] In agreement with a very recent report,[4] we have obtained epirotenone (VIIa) crystalline as the half-methanol solvate and possessing a much higher rotation than earlier samples. A recent claim has been made [5] that if mutarotenone is melted for five minutes at 190° and is then crystallised from ethanol an almost quantitative yield of natural rotenone results. This would necessitate almost complete conversion of the 6aα,12aα,5′β- into 6aβ,12aβ,5′β-material and would be very difficult to explain. The claim seems incorrect as the optical activity of mutarotenone is virtually unaffected by heat; also, destruction of the optical activity at the 5′-centre by acid isomerisation to the isorotenone series gives products from both heated and unheated mutarotenone which have similar slight rotations. It is crystallisation from ethanol (or chloroform–methanol) which effects separation of natural rotenone from epirotenone.

The formation of rotenol (XV—XVIa) and derritol (XIVa) [6,7] when rotenone is treated with zinc and alkali is readily explained as involving the ion (Va). Rotenol arises from 1,4-reduction of the latter, whilst formation of derritol is rationalised as attack as in (XIa) to give (XIIa) which by prototropic shift gives (XIIIa). Reaction is completed by retroaldol condensation. As formulated, rotenol must be a mixture of two diastereoisomers but, although this substance has been mentioned on a number of occasions in the literature (m. p. 120°), its homogeneity has never been questioned. By careful crystallisation it has been possible to resolve the mixture, one diastereoisomer having m. p. 141—143°, $[\alpha]_D^{21}$ −245°, the other m. p. 90°, $[\alpha]_D^{21}$ +33°. These are not epimerised at position 6a by 1 hour's boiling with 5% ethanolic sulphuric acid but dilute alkali rapidly racemises them to an equilibrium mixture and, from this, " ordinary " 12aα,12aβ-rotenol is readily isolated. Connexion of the stereochemical formulæ (XVa) or (XVIa) with each diastereoisomer is not at present possible. (+)-Rotenol has a positive Cotton effect, and

[4] Takahashi, Fukami, and Nakajima, *Bull. Agric. Chem. Soc. Japan*, 1960, **24**, 123.
[5] Miyano and Matsui, *Chem. Ber.*, 1958, **91**, 2044.
[6] Butenandt, *Annalen*, 1928, **464**, 253.
[7] LaForge and Smith, *J. Amer. Chem. Soc.*, 1929, **51**, 2574.

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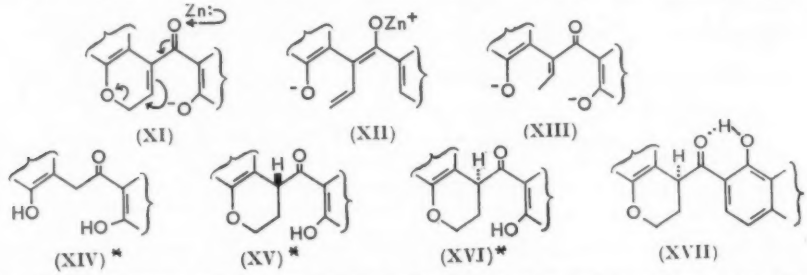
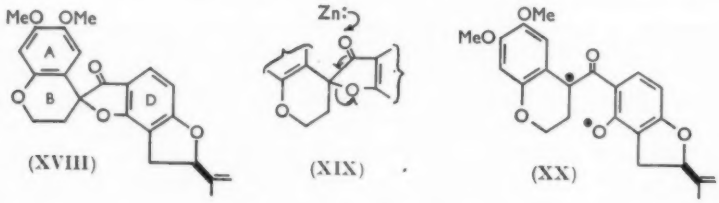
(−)-rotenol a negative one,† but the two curves are not enantiomorphic because of the superimposed constant plain curve due to the 5′-centre.

The first claim to have isolated the 6a,12a-dehydrorotenol (Va, protonated) was made by Haller and LaForge [8] who obtained a white crystalline product, m. p. 124°, when rotenol was treated with alkaline ferricyanide. Later [9] the claim was withdrawn and ring C (cf. XVIII) was thought to be five- or seven-membered. In our hands this reaction gives a powdery mixture of two diastereoisomers (5′β) from which one, corresponding with



* *o*-Phenolic ketones of this type are powerfully chelated, as shown by the position of their hydroxyl (emerging as a skirt from both sides of the C–H stretching complex) and ketone bands in the infrared spectra, thus (XVI) should conventionally be represented as (XVII), but this elaboration is here omitted.

the above, can be crystallised. Its structure is now dealt with. The 12-keto-grouping is intact for it can be reduced with borohydride and the resulting benzylic alcohol can be oxidised back to the original ketone with manganese dioxide. The ketone is not enolisable and its stretching vibration (1704 cm.$^{-1}$) supports a five-membered environment (rotenone 1674 cm.$^{-1}$). No hydroxyl group is present. This suggests that the spiro-structure (XVIII) is correct. Isorotenone is similarly converted into a spiro-compound analogous to (XVIII) ($\nu_{max.}$ 1709 cm.$^{-1}$; cf. isorotenone 1680 cm.$^{-1}$) but, being a racemate, this is at once obtained crystalline (cf. the structure of isorotenolone C,[10] which has $\nu_{max.}$ 1706 cm.$^{-1}$). Proposal (XVIII) is confirmed since the substance,[8] and its analogue from isorotenone, give rotenol and isorotenol respectively, without formation of derritol and isoderritol, when treated with zinc and alkali. This is clear from the representation (XIX). The spiro-compound (XVIII) and its relative are presumably formed in one-electron



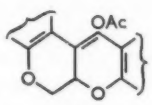
transfer reactions *via* a mono- or a di-radical (XX).[11] Treatment of isorotenol with lead tetra-acetate also gives some of the spiro-compound (iso-series, as XVIII). Refluxing of rotenol with alkaline manganese dioxide in dioxan gives both the spiro-compound (XVIII) (by a radical reaction) and 6a,12a-dehydrorotenone. Presumably, to account

† We thank Professor W. Klyne for this information.

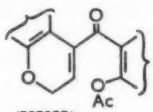
[8] Haller and LaForge, *J. Amer. Chem. Soc.*, 1931, **53**, 2271.
[9] Haller, *J. Amer. Chem. Soc.*, 1932, **54**, 2126.
[10] Crombie and Godin, preceding paper.
[11] Scott, *Proc. Chem. Soc.*, 1958, 195, and references cited there.

for the latter, 6a,12a-dehydrorotenol (Va; protonated) is formed which cyclises to mutarotenone and is then dehydrogenated (see below).

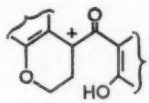
Jennen's work [2] is of particular interest in connection with the isolation of 6a,12a-dehydro-compound (Va; protonated). He reported that, if rotenone in benzene is treated with sodium or with solid sodium hydroxide, a solution of a sodium compound is formed which, if poured into acetylating mixture, gives a yellow acetate, m. p. 134°.



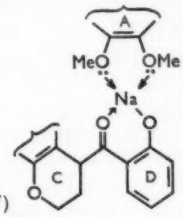
(XXI)



(XXII)



(XXIII)



(XXIV)

Degradative studies were not reported but because the ultraviolet spectrum of this substance differed from that of the enol acetate (XXIa) of rotenone, the new acetate was formulated as (XXIIa), *i.e.*, the trapped form of the intermediate in the racemisation of rotenone; the parent phenol (cf. Va) could not be isolated pure. More extensive investigation now supports Jennen's view and it has proved possible to isolate the pure, yellow, crystalline intermediate (Va; protonated), m. p. 96°, which is chelated (cf. XVII) and can be acetylated to give the acetate (XXIIa). In order that racemates rather than diastereoisomeric pairs should be formed during some chemical transformations, the acetate (XXIIc) from isorotenone has also been made. Jennen's preparation of the sodium compound is of interest. In a solvent of low dielectric constant the sodium compound will exist as an ion pair, inhibiting recyclisation, and either the ion pair of (V), (IV), or (VI) might accumulate. Jennen suggested that his benzene solution contained a polymeric system (XXIV) based on 4-co-ordinated sodium and this would explain why a derivative of (V) is preferred to one of (IV) or (VI) from which the co-ordination complex cannot be formed.

The acetate (XXIIa) showed acetyl (1761 cm.$^{-1}$) and conjugated ketone (1652 cm.$^{-1}$) bands in the infrared spectrum and absorbed 2 mol. of hydrogen catalytically to give an acetate which when hydrolysed gave the known 6′,7′-dihydrorotenol (XV—XVIb). This establishes the skeleton and makes the 6a,12a-position of the double bond likely. This position was confirmed by acetylating rotenol and dehydrogenating the product with manganese dioxide in refluxing acetone, which gave the acetate (XXIIa) by rational synthesis. The structure and the place of compounds of the 6a,12a-dehydrorotenol type in rotenoid chemistry is illustrated by the following results.

When treated with the weak base sodium acetate in ethanol 6a,12a-dehydrorotenol (Va, protonated; 5′β) is readily converted into mutarotenone. The acetate (XXIIa) of this dehydro-compound and the corresponding isorotenone derivative (XXIIc) give mutarotenone and (±)-isorotenone, respectively, when refluxed with aqueous pyridine. When refluxed with acid, however, 6a,12a-dehydrorotenol and its acetate give the diastereoisomeric pair of spiro-compounds (XVIII) from which one was isolated crystalline: similarly 6a,12a-isodehydrorotenol acetate (XXIIc) gave the racemic spiro-compound (cf. XVIII). The course of this acid-catalysed cyclisation must be different from that involved in the other preparations of the spiro-compounds and is explained as requiring formation of the tertiary carbonium ion (XXIII) stabilised by the ether-substituted ring A despite the adjacent carbonyl group. It has been necessary to postulate this type of intermediate for the acid-catalysed conversion of *trans*-B/C 12a-methoxy-rotenoids into the *cis*-B/C 12a-methoxyrotenoids [12] and the formation of a spiro-compound in the peltogynol series [13] may be related to it. Hydrolysis of 6a,12a-dehydrorotenol acetate (XXIIa)

[12] Büchi, Crombie, Godin, Kaltenbronn, Siddalingaiah, and Whiting, *J.*, 2843.
[13] Chan, Forsyth, and Hassall, *J.*, 1958, 3174.

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with sodium hydroxide gives mutarotenone, but this rapidly undergoes secondary reactions under the strongly alkaline conditions. From the product, a substance m. p. 128—129°, isomeric with rotenone, was isolated in small yield.

If the views developed above are correct, the same substance ought to be obtained merely by treating rotenone with sodium hydroxide solution. This was so. Further, the substance was a mixture of separable diastereoisomers having nearly identical infrared solution spectra. One diastereoisomer had m. p. 150—151°, $[\alpha]_D^{20}$ +203°, the other m. p. 122—123°, $[\alpha]_D^{20}$ −235°, and they represent the 12aβ,5′β (IXa) and the 12aα,5′β-form (Xa) of 6,6a-dehydrorotenol, the two possible diastereoisomers of Cahn's proposed intermediate (keto-form) in the racemisation of rotenone.* Their origin clearly lies in prototropic shifting of the double bond of the true intermediate (Va). (−)-Isorotenone similarly gives a racemic 6,6a-dehydroisorotenol (IX—Xc) which, when boiled with potassium carbonate in wet acetone, yields (±)-isorotenone. As direct intermediates in the racemisation of rotenoids the 6,6a-dehydrorotenols are not acceptable, for when either diastereoisomer was boiled with saturated ethanolic sodium acetate much remained unchanged (though becoming racemised at position 12a). The structure of the two 6,6a-dehydrorotenols is shown by the following facts. Treatment with pyridine and acetic anhydride gives an acetyl derivative (with epimerisation at position 12a) which can be catalytically hydrogenated to 6′,7′-dihydrorotenol acetate and hydrolysed to 6′,7′-dihydrorotenol (XV—XVIb), thus establishing the skeleton. The chelated hydroxyl group is shown by the ferric chloride reaction and infrared data [1651 cm.$^{-1}$ (chelated ketone)]. In view of the skeletal evidence and the existence of an asymmetric centre other than 5′, the double bond in ring B must be at 6,6a. Catalytic hydrogenation of the diastereoisomer of m. p. 150—151° gives 6′,7′-dihydrorotenol having $[\alpha]_D^{20}$ −196°, whilst the diastereoisomer of m. p. 122—123° gives 6′,7′-dihydrorotenol of $[\alpha]_D^{19}$ −86°. Hydrogenation of the rotenol diastereoisomer, m. p. 141—143° (above), gives 6′,7′-dihydrorotenol, $[\alpha]_D^{22}$ −214°. This shows that the latter is configuratively the same as the 6′,7′-dihydrorotenol of m. p 150—151°, though the absolute configuration at position 12a is not known. Some racemisation at position 12a occurs during hydrogenation of compounds (IX) and (X) (nearly complete for one diastereoisomer), and effective double-bond migration from position 6,6a to 6a,12a on the catalyst may be implicated.

Other information which is readily accommodated by acceptance of the ion (V) as being formed in alkaline solutions of rotenoids is the isolation of dehydronetoric (toxicaric) acid (XXV) on oxidation of rotenone or toxicarol by alkaline peroxide.[3a,14,15] Further, rotenoids give a different series of compounds when oximated with hydroxylamine hydrochloride in the presence of sodium hydroxide from those obtained by oximation with the same reagent in the presence of sodium acetate.[6] The latter are considered to be normal oximes (XXVI), and the former isoxazolines (iso-oximes)[3,6,16] (XXVII) which would arise from attack on the ion (V) as in (XXIX). Spectral information supports the constitution of these derivatives. Rotenoid oximes (XXVI) have "free" hydroxyl bands near 3592 cm.$^{-1}$ (cf. α-tetralone oxime, 3595 cm.$^{-1}$), whilst the iso-oximes have strongly chelated hydroxyl groups: there are two chelated bands near 3170 and 3080 cm.$^{-1}$ (CaF_2, CCl_4, $<\sim$0·005M). The presence of the two bands suggests that the two tautomers (XXVII) and (XXVIII) may be present.

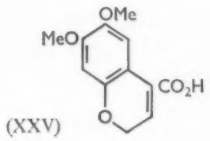
Cahn and his colleagues have carried out comparative studies of the reactions of rotenone and toxicarol.[1] The work on toxicarol provides an interesting complement to

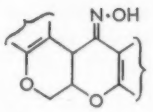
* On hearing of this, Professor S. H. Harper recently recalled work (unpublished) he had done in 1942 on the alkaline treatment of rotenone. His original notes show that he isolated the pure diastereoisomer, m. p. 151°, but an adequate formulation could not be arrived at. All his observations agree with the structure above and we thank him for this information.

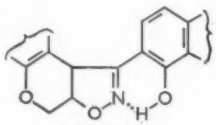
[14] Butenandt and Hilgetag, *Annalen*, 1932, **495**, 172.
[15] Clark, *J. Amer. Chem. Soc.*, 1932, **54**, 2537.
[16] LaForge and Haller, *J. Amer. Chem. Soc.*, 1932, **54**, 810.

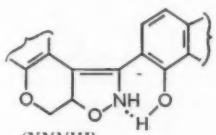
XUM

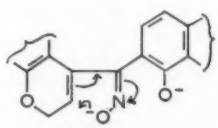
that described above, and rationalisation is now attempted. (±)-α-Toxicarol (XXX) is readily equilibrated with (±)-β-toxicarol (XXXII) when treated with potassium carbonate in wet acetone, and the structure of both compounds is securely founded.[1,17] This provides good evidence for the existence of a 6a,7-opened intermediate which we consider to be (XXXI)


(XXV)

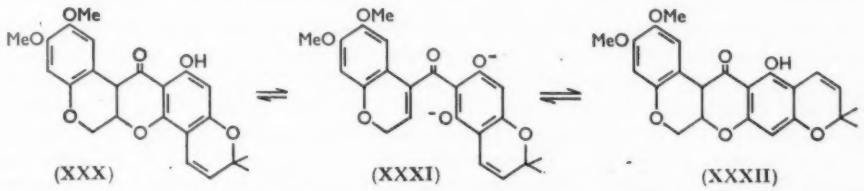

(XXVI)


(XXVII)


(XXVIII)


(XXIX)

or the monoprotonated form, and new terms have to be added to the scheme of alkaline behaviour on p. 2877. When a benzene solution of natural (−)-α-toxicarol * is treated with a little methanolic potassium hydroxide, there is an immediate shift in rotation from −66° to +276°; thereafter there is a steady fall towards zero (the behaviour of sumatrol is related).[1,18] If, immediately after addition of alkali, the solution is acidified, unracemised (−)-α-toxicarol is recovered.[1] These phenomena are said [1] to be due to enolisation of the ketone prefatory to 6a,7-cleavage to give the species (II). In our view the immediate positive surge in the rotation is due to ionisation of the 11-phenolic hydroxyl; racemisation then proceeds *via* the di-ion (XXXI). The immediate shift of the main ultraviolet maximum of toxi-


(XXX) (XXXI) (XXXII)

carol from 272·5 mμ in ethanol to 280 mμ in M/20-aqueous-alcoholic sodium hydroxide has also been put down to enolisation,[1] but it is due to phenolic ionisation. Thus the spectrum of (±)-12a-hydroxytoxicarol (XXXIII; R = H), although the compound cannot enolise, suffers a shift of $\lambda_{max.}$ from 273 to 283 mμ under similar conditions. On the other hand, (±)-12a-hydroxytoxicarol 11-acetate (XXXIII; R = Ac) has $\lambda_{max.}$ 270 mμ in neutral ethanol and in alkaline ethanol if the peak is measured at once (gradually the maximum shifts to 280 mμ as the acetate is hydrolysed). Recognition of this simple ionisation process helps us to understand further experimental facts.

Rotenone is methylated by methyl sulphate in boiling acetone containing water if potassium carbonate or potassium hydroxide is present: the product is the 6a-racemised acid-labile enol ether (XXXIVa).[19] However, when (±)-α- or (±)-β-toxicarol is similarly treated the product, in good yield, is the acid-stable ether (XXXVd). Potassium carbonate, when added to (−)-α-toxicarol in aqueous acetone, causes the characteristic

* The prefix (−) refers to benzene solution; the sign changes in certain other solvents.

[17] George and Robertson, *J.*, 1937, 1535.
[18] Harper, *J.*, 1939, 812.
[19] Cahn, Phipers, and Boam, *J.*, 1938, 734.

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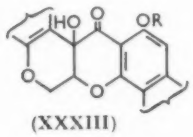
strong positive surge of rotation followed by a slow decline to zero and is obviously basic enough largely to ionise the $C_{(11)}$-phenol group. Removal of the 12a-proton from ionised α-toxicarol leads to the enolate (XXXVI) but the juxtaposition of the two negative charges must greatly destabilise this relative to the derivative (XXXVII). Consequently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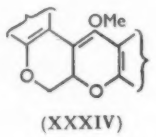
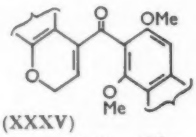
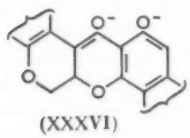
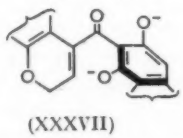
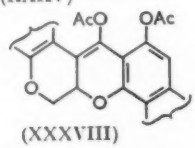

(XXXIV)


(XXXV)


(XXXVI)

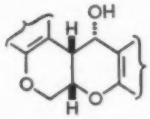

(XXXVII)

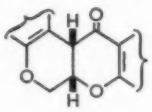

(XXXVIII)

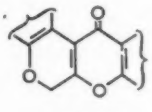
the relative stabilities and equilibrium concentrations of species (IV) and (V) are likely to be very different in the cases of rotenone and toxicarol, attack on the open form (XXXVII) being much more likely in the latter case. In the open form, the aromatic ring D can rotate to relieve unfavourable interaction between the carbonyl dipole and the phenoxide ion.

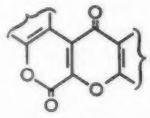
Acetylation of rotenone by refluxing sodium acetate–acetic anhydride gives the enol acetate (XXIa) with racemisation at position 6a; although formation of the ion (V) must be invoked to account for racemisation, the major acetylation attack is on ions (IV) and (VI). If (—)-α-toxicarol [or (—)-dihydro-α-toxicarol, for which better experimental evidence is available [19]] is treated for a short time with the reagent, the optically active 11-phenol monoacetate can be isolated, but on long treatment the racemised diacetate (XXXVIII) is obtained. Sodium acetate in acetic anhydride must be a much weaker base than potassium carbonate in wet acetone and the stationary concentration of phenoxide ion will be very low [ethanolic sodium acetate causes no positive rotatory surge when added to (—)-α-toxicarol]. The phenol can be acetylated with little racemisation. Longer treatment causes racemisation of this acetate *via* the open form (V) but the stationary concentration of the latter need only be low and ordinary enol-acetylation, as in the case of rotenone, takes precedence. The diacetate of the open form of toxicarol [corresponding to (XXXV)] can be made by treating toxicarol with sodium hydroxide in benzene and pouring the mixture into acetylating mixture.[2]

A characteristic reaction of rotenoids is their 6a,12a-dehydrogenation, usually carried out by treatment with iodine and potassium acetate in ethanol, which causes α-iodination and dehydrohalogenation.[20] A driving force is gain of pyrone resonance energy and perhaps relief of angle strain. We find active manganese dioxide to be an excellent


(XXXIX)


(XL)


(XLI)


(XLII)

reagent for such dehydrogenations, and other levels of oxidation of the B/C system can be effected. Starting with hydroxy-compound (XXXIX) it is possible to oxidise to the rotenone level (XL), though it is difficult to prevent some over-oxidation to (XLI). The conversion (XL ⟶ XLI) is very smooth and proceeds in higher yield than by earlier

[20] LaForge, Haller, and Smith, *Chem. Rev.*, 1933, **12**, 181.

methods. In some 11-hydroxy-rotenoids (α- and β-toxicarol) oxidation proceeds still further to the rotenononone level (XLII). The conversion (XL) ⟶ (XLI) is a surface reaction and the *cis*-arrangement of the two hydrogens on the manganese dioxide may be helpful. Earlier preparations of compounds of the rotenononone type (XLII) have given poor yields, but we find that the conversion of 6a,12a-dehydro-compounds (XLI) can be satisfactorily carried out by oxidation with lead tetra-acetate. 6a,12a-Dehydro-rotenoids are useful intermediates in the degradation of rotenoids as they are hydrolysed by base to compounds of the derrisic acid type which can be degraded further.

Experimental

For general experimental procedures see p. 2852. Rotations are for benzene solutions unless otherwise stated.

6aβ,12aβ,5′β- *and* 6aα,12aα,5′β-*Rotenone Mixture* (*Mutarotenone*).—Natural rotenone (25 g.), anhydrous sodium acetate (125 g.), and ethanol (500 ml.) were heated under reflux for 4 hr. The mixture was poured into water and kept at 0° for 12 hr. Crystalline mutarotenone (24·9 g.), m. p. 138—142°, $[\alpha]_D^{25}$ −99·7° (*c* 2), was filtered off. A specimen of the latter (1 g.) was refluxed with sodium acetate (5 g.) in ethanol (25 ml.) for 3 hr. more: isolation gave mutarotenone (0·96 g.), $[\alpha]_D^{25}$ −101° (*c* 1·4).

Mutarotenone (420 mg.; $[\alpha]_D^{25}$ −99·7°) was kept at 60° for 1 hr. with concentrated sulphuric acid (4 ml.) and acetic acid (3 ml.), then poured into water. Isorotenone, $[\alpha]_D^{21}$ −9·7° (*c* 1·65), was obtained. A second and a third isomerisation gave $[\alpha]_D^{25}$ −3·0° (*c* 2·64 in $CHCl_3$) and $[\alpha]_D^{25}$ −1·1° (*c* 1·29 in C_6H_6).

The same mutarotenone (5·03 g.) was crystallised from ethanol as follows: first crystallisation (2·01 g.), $[\alpha]_D^{21}$ −208 (*c* 1·9); third crystallisation (1·10 g.), m. p. 164·5—166°, $[\alpha]_D^{21}$ −218° (*c* 1·2) {natural rotenone has m. p. 165—166°, $[\alpha]_D^{20}$ −228° (*c* 2·22)}. By crystallisation from benzene–ether, material of m. p. 147°, $[\alpha]_D^{23}$ −144° (*c* 2·24), was obtained but no stationary value of rotation and m. p. is reached by crystallisation from benzene–ether, ethanol, methanol–chloroform, or carbon tetrachloride until pure (−)-rotenone is isolated (lit.,[1] for mutarotenone, m. p. 145—146°, $[\alpha]_D$ −80° to −86°).

Mutarotenone, $[\alpha]_D^{25}$ −99·7°, was heated in a " Pyrex " tube at 20° above its m. p. for 20 min.[5] and then had $[\alpha]_D^{22}$ −104° (*c* 2·3). When isomerised with concentrated sulphuric and acetic acid the heated product (424 mg.) gave isorotenone (410 mg.), $[\alpha]_D^{22}$ −9·85° (*c* 2·3). Parallel crystallisation (once) of unheated and heated mutarotenone (1 g.) from ethanol gave rotenone (0·4 g.), $[\alpha]_D^{21}$ −208° (*c* 1·9), and (0·3 g.), $[\alpha]_D^{21}$ −187° (*c* 0·5), respectively.

6aα,12aα-5′β-*Rotenone* (" d-*Epirotenone* ").—Mutarotenone (100 g.) was crystallised from carbon tetrachloride, and the mother-liquors were evaporated and crystallised from benzene–ether (2 weeks). After filtration, the filtrate was evaporated, dissolved in ether, and kept for several weeks. The product was again filtered and the filtrate on evaporation gave 6aα,12aα,5′β-rotenone concentrate, a glass, $[\alpha]_D^{18}$ +25·6° (*c* 0·74). Cahn, Phipers, and Boam [1] report $[\alpha]_D$ +30° for their specimen but recently Nakajima and his colleagues [4] have reported m. p. 89—91°, $[\alpha]_D$ +72·5°, for the methanol solvate of *d*-epirotenone. A crystal of this material was kindly supplied by Professor Nakajima but had decomposed (softened 90°, m. p. 144°) and failed to cause crystallisation of the glass from methanol.

The glass, $[\alpha]_D^{18}$ +25·6°, was kept in ether for some weeks at 20° and the mixture was filtered. The filtrate was evaporated, dissolved in methanol, kept for some days, and then filtered. This methanol crystallisation and rejection of the crystalline material was repeated twice more. Finally the filtrate was treated with charcoal and kept at 0°, to give 6aα,12aα,5′β-rotenone (VIIa), m. p. 86—89°, $[\alpha]_D^{21}$ +56° (*c* 2), as the methanol solvate; further crystallisation from methanol gave material of m. p. 90°, $[\alpha]_D^{18}$ +75·6° (*c* 0·6) (Found: C, 68·85; H, 5·9. Calc. for $C_{23}H_{22}O_6,\frac{1}{2}CH_3{\cdot}OH$: C, 68·8; H, 5·9%). The infrared solution spectrum was closely similar to that of natural rotenone.

Diastereoisomers of Rotenol (XVa and XVIa).—Rotenone (40 g.), zinc dust (80 g.), and ethanol (1·2 l.) were heated to the b. p. and 10% aqueous potassium hydroxide (400 ml.) was added; the mixture was stirred and refluxed for 3½ hr. and then filtered. The filtrate was acidified with 2N-hydrochloric acid and extracted with ether. The ethereal extracts were extracted with 2N-potassium hydroxide and evaporated, to give the " neutral " fraction. The

basic extract contained derritol and in some cases was worked up for this. In one such experiment the acidic fraction was dissolved in a minimum of hot methanol and cooled to 0°, to give derritol, m. p. 160—161°, $[\alpha]_D^{20\cdot5}$ −74° (*c* 2·1 in $CHCl_3$) {lit.,[7] m. p. 164°, $[\alpha]_D^{20}$ −66·2° (*c* 3·4 in $CHCl_3$}. Four further crops of derritol were isolated but the fifth crop was crude rotenol, m. p. 112—114°, $[\alpha]_D^{21}$ −116° (*c* 2·4) (correct infrared spectrum). Rotenol is not insoluble in alkali but is extracted only slowly from ethereal solution by aqueous base.

The " neutral " fraction crystallised from methanol to give " ordinary " rotenol (13 g.), m. p. 114·5—116·5°, $[\alpha]_D^{19}$ −120° (*c* 1·81), (m. p. 120° on recrystallisation) {lit.,[6,7,21,22] m. p. 115—120°, 119°, 120° $[\alpha]_D^{20}$ −77·3° (*c* 3·98 in $CHCl_3$)}. The material was crystallised six times from methanol, to give (−)-5′β-*rotenol*, m. p. 141—143°, $[\alpha]_D^{21}$ −245° (*c* 2·52) (Found: C, 69·7; H, 6·2; O, 24·15. $C_{23}H_{24}O_6$ requires C, 69·7; H, 6·1; O, 24·2%). The mother-liquors were repeatedly crystallised from methanol and finally gave (+)-5′β-*rotenol*, m. p. 90°, $[\alpha]_D^{20}$ +33° (*c* 0·7) (Found: C, 69·45; H, 6·0%). The chloroform solution spectra of (+)-, (−)-, and " ordinary " rotenol were virtually identical, but as mulls they could be differentiated.

Racemisation of (+)- *and* (−)-5′β-*Rotenol*.—(+)-5′β-Rotenol (10·97 mg.) in acetone (0·6 ml.) was treated with 0·02% ethanolic potassium hydroxide (0·6 ml.). Polarimetric rotations were followed, $[\alpha]_D^{20}$ becoming constant at −64·5°. (−)-5′β-Rotenol (11·37 mg.) was treated similarly, giving final $[\alpha]_D^{20}$ −64·5°.

(+)-Rotenol (20 mg.) and anhydrous sodium acetate (50 mg.) in ethanol (2 ml.) were refluxed for 4 hr. Water was added and, on cooling to 0°, " ordinary " rotenol (19 mg.), m. p. and mixed m. p. 114—117°, $[\alpha]_D^{19}$ −104° (*c* 1·82), was obtained.

(−)-Rotenol (500 mg.), treated with sodium acetate (3 g.) in ethanol as above, gave " ordinary " rotenol (460 mg.), m. p. and mixed m. p. 118—119°, $[\alpha]_D^{21}$ −110·5° (*c* 2).

(−)-Rotenol (250 mg.) was refluxed for 1 hr. with 5% ethanolic sulphuric acid (50 ml.). On cooling and filtration an almost theoretical yield of unchanged (−)-rotenol, m. p. and mixed m. p. 142—143°, $[\alpha]_D^{22}$ −238° (*c* 1·75), was recovered.

(−)-6′,7′-*Dihydro*-5′β-*rotenol*.—(−)-5′β-Rotenol (105 mg.) in ethyl acetate (15 ml.) was hydrogenated over palladium–barium sulphate (80 mg.), to give (−)-6′,7′-dihydro-5′β-rotenol (90 mg.), m. p. 137—138°, $[\alpha]_D^{22}$ −214° (*c* 1·74) (see below).

5′β-*Diastereoisomers of the Spiro-compound* (XVIII).—(*a*) Warm potassium ferricyanide (900 mg.) in water (10 ml.) was added to rotenol (500 mg.) in 5% ethanolic potassium hydroxide. The mixture was shaken overnight, poured into water, and continuously extracted with ether. Evaporation of the ether left a gum which was chromatographed from benzene on alumina (N5) and then dissolved in methanol and poured into water, to give a powder, m. p. 75—80°, containing the two 5′β-diastereoisomers (Found: C, 69·8; H, 5·6. Calc. for $C_{23}H_{22}O_6$: C, 70·05; H, 5·6%), $\nu_{max.}$ 1704 (C=O), 1623, 1603, 1502 (aryl), and 913 (isopropenyl) cm.$^{-1}$. There was no hydroxylic absorption and no coloration with ferric chloride. Crystallisation from ethanol gave one diastereoisomer, m. p. 119—121°, $[\alpha]_D^{20}$ −88° (*c* 0·64) (lit.,[8] m. p. 124°).

(*b*) Rotenol (314 mg.) was heated under reflux with alkaline active manganese dioxide (3 g.) in dioxan (15 ml.) for 3 hr. Filtration and addition of a little water to the filtrate gave 6a,12a-dehydrorotenone (60 mg.), m. p. and mixed m. p. 219—222° (infrared confirmation). The filtrate was further diluted with water and extracted with chloroform. Evaporation of the extract gave the spiro-compound (XVIII) (95 mg.), amorphous, identified by its infrared spectrum (mull). Shaking at 20° with the above reagent gave mainly unchanged rotenol.

Racemic Spiro-compound (XVIII, *but of the Isorotenone Series*).—(*a*) Isorotenol (2 g.) was treated with potassium ferricyanide (3·6 g.) in alkali as above. The mixture was acidified and chromatographed from benzene on alumina (N1) to give, after crystallisation from methanol, the *spiro-racemate* of the isorotenone series (320 mg.) as plates, m. p. 126° (Found: C, 69·7; H, 5·85. $C_{23}H_{22}O_6$ requires C, 70·05; H, 5·6%), $\lambda_{max.}$ 240 (4·72), 246i (4·65), 264i (4·02), 281 (4·06), 290 (4·02), and 335 (3·74) mμ, $\nu_{max.}$ 1709 (C=O), 1634, 1597 and 1504 cm.$^{-1}$ (aryl).

(*b*) Isorotenol (1 g.) was treated with lead tetra-acetate (5 g.) in glacial acetic acid (25 ml.) for 2 hr. The solution was poured into water, and the whole crude product was chromatographed from benzene on alumina (N1). The infrared spectrum (chloroform) of the main product showed that spiro-compound had been formed directly ($\nu_{max.}$ 1709 cm.$^{-1}$ and general character of the spectrum) but acetoxy-substituted material was also present [$\nu_{max.}$ 1750 cm.$^{-1}$ (Ac)]. The product was shaken for 5 days with 10% methanolic potassium hydroxide (10 ml.) then

[21] Takei, Miyajima, and Ono, *Ber.*, 1932, **65**, 279.
[22] Haller and LaForge, *J. Amer. Chem. Soc.*, 1931, **53**, 3426.

heated to the b. p. and poured into dilute hydrochloric acid. The precipitate was filtered off, chromatographed as above, and crystallised from methanol to give the spiro-racemate, plates, m. p. and mixed m. p. with the above sample 125°. Identity was confirmed by the infrared spectrum (mull). Apart from direct formation, the spiro-compound may also originate by hydrolysis of 12a-acetoxyisorotenol and subsequent cyclisation. From a structural point of view both routes have the same import.

Reduction of Spiro-compound (XVIII) *and Oxidation of the Reduction Product.*—The spiro-compound (500 mg.) in ethanol (30 ml.) was treated at 60° for 1 hr. with potassium borohydride (250 mg.) and potassium hydroxide (100 mg.) in water (10 ml.). After 5 hr. at 20° the solution was poured into water, and the amorphous solid was isolated (400 mg.). It showed hydroxyl but no carbonyl absorption in the infrared spectrum (mull). The alcohol (400 mg.) was shaken for 12 hr. with active manganese dioxide (2 g.) in acetone (10 ml.). The whole was filtered and the manganese dioxide was washed with chloroform. Evaporation of the filtrate and washings gave a powder identical with the starting spiro-ketone (mull infrared spectrum).

Treatment of the Racemic Spiro-compound [*as* (XVIII), *but of the Isorotenone Series*] *with Zinc and Alkali.*—The spiro-compound (250 mg.), zinc dust (1 g.), 95% ethanol (10 ml.), and 40% aqueous potassium hydroxide (2·5 ml.) were refluxed for 2 hr. The mixture was filtered, acidified, and extracted with ether. These extracts were treated to afford acidic and neutral fractions. When crystallised from methanol the neutral gum (195 mg.) gave isorotenol (115 mg.), m. p. and mixed m. p. 129—130°; identity was confirmed by infrared spectra (mull and solution). The acid fraction gave only impure isorotenol (10 mg.), identified spectroscopically.

Authentic isorotenol, m. p. 131°, was made by isomerisation of rotenol with sulphuric acid in glacial acetic acid (lit.,[8] m. p. 131°).

6a,12a-*Dehydrorotenol* (Va) *and its Acetate* (XXIIa).—Rotenone (5 g.) in dry benzene (100 ml.) was added to sodium wire (3 g.) under benzene (300 ml.). The mixture was then refluxed under dry nitrogen for 4 hr. and the pale yellow solution was decanted, washed with 4N-hydrochloric acid and then with chalk suspension, and dried ($MgSO_4$). Evaporation gave a gum which, when dissolved in ethanol and kept at 0° for 60 hr., gave 6a,12a-*dehydrorotenol* (3·8 g.) as yellow needles, m. p. 94—96° (from methanol), $[\alpha]_D^{17}$ −75° (*c* 1·8) (Found: C, 70·1; H, 5·7. $C_{23}H_{22}O_6$ requires C, 70·05; H, 5·6%), $\lambda_{max.}$ 305 (4·31), 315i (4·29) mμ, $\nu_{max.}$ 1646 (chelated unsaturated ketone), 1616, 1590i, and 1497 (aryl) cm.$^{-1}$. The compound gave a red ferric reaction. Jennen, using a different technique, obtained impure material, m. p. 76—78°. 6a,12a-Dehydrorotenol (150 mg.) was kept at 20° for 12 hr. with acetic anhydride (3 ml.) and pyridine (2 ml.). Working up gave the acetate (125 mg.), m. p. 138° alone or mixed with the specimen recorded below (infrared confirmation).

Rotenone (3 g.) was added to sodium hydroxide pellets (45 g.) and stirred under dry benzene (300 ml.) at 60° in a nitrogen atmosphere. The mixture was heated for 7 hr. (becoming blood-red) and then decanted into acetic anhydride (400 ml.) containing fused, powdered sodium acetate (45 g.). After refluxing for 5 hr. in nitrogen the mixture was poured on ice, and the benzene layer isolated and evaporated to a gum which crystallised from methanol (charcoal), to give 6a,12a-dehydrorotenol acetate (2·37 g.), m. p. 138—139° (Found: C, 68·5; H, 5·8. Calc. for $C_{25}H_{24}O_7$: C, 68·80; H, 5·55%), $[\alpha]_D^{22}$ −84·5° (*c* 1·76), $\lambda_{max.}$ 284 (4·19) mμ, $\nu_{max.}$ 1761 (Ac), 1652 (unsatd. ketone), 1613, and 1506 (aryl) cm.$^{-1}$. Chromatography from benzene on alumina raised the m. p. to 139—140°. Jennen [2] gives m. p. 134°, $[\alpha]_D$ −74°, $\lambda_{max.}$ 284 mμ (4·19). An identical product was obtained by using sodium wire (1 g.) in place of sodium hydroxide.

6a,12a-*Dehydroisorotenol.*—Isorotenone (3 g.) was treated with sodium hydroxide (45 g.) in benzene as above, and the resulting solution was acetylated as above. Working up gave 6a,12a-*dehydroisorotenol acetate* (500 mg.), m. p. 161·5—162·5° (Found: C, 68·75; H, 5·65%), $\lambda_{max.}$ 244 (4·55), 280 (4·09) and 314 (3·81) mμ, $\nu_{max.}$ (mull) 1761 (Ac), 1650 (unsatd. ketone), 1616, 1587, 1572, and 1513 (aryl) cm.$^{-1}$. In an experiment with isorotenone (12 g.) and sodium wire (3 g.) the yield was 4 g.

6a,12a-*Dehydrorotenol Acetate by Dehydrogenation of Rotenol Acetate.*—Rotenol (250 mg.) was treated with pyridine (1·5 ml.) and acetic anhydride (2 ml.) for 12 hr. Working up and chromatography gave rotenol acetate (two diastereoisomers) as an amorphous solid (Found: C, 68·65; H, 5·85. Calc. for $C_{25}H_{26}O_7$: C, 68·5; H, 5·95%), $[\alpha]_D^{20}$ −103° (*c* 1·48), $\lambda_{max.}$ (in ethanol or ethanolic 0·01N-potassium hydroxide) 290 (4·24) mμ, $\nu_{max.}$ 1762 (Ac), 1687 (C=O) cm.$^{-1}$. Earlier failure to obtain this material crystalline has been reported.[16]

XUM

Rotenol acetate (350 mg.) was heated under reflux for 2·5 hr. with active manganese dioxide in acetone (25 ml.). Working up and crystallisation from methanol gave dehydrorotenol acetate (XXIIa) (50 mg.), m. p. and mixed m. p. 138°. An infrared spectrum (mull) confirmed the identity.

Hydrogenation of 6a,12a-*Dehydrorotenol Acetate.*—The acetate (225 mg.) was hydrogenated in ethyl acetate (15 ml.) over 5% palladium–barium sulphate (2 mols. of H_2 absorbed). Working up gave amorphous 6′,7′-dihydrorotenol acetate (200 mg.). Rotenol acetate (240 mg.), similarly hydrogenated, absorbed 1 mol. of hydrogen, giving the amorphous *6′,7′-dihydrorotenol acetate* (220 mg.) with infrared mull spectrum closely similar to that of the first specimen (Found: C, 68·25; H, 6·5. $C_{25}H_{28}O_7$ requires C, 68·15; H, 6·4%), $\lambda_{max.}$ 282 (3·92) and 330 (3·85) mμ $\nu_{max.}$ 1761 (Ac), 1658 (C=O) cm.$^{-1}$.

6′,7′-Dihydrorotenol acetate (first specimen) was refluxed for 20 min. with 5% ethanolic sulphuric acid (25 ml.). Working up gave a gum (140 mg.) which crystallised from methanol to give 6′,7′-dihydrorotenol (60 mg.), m. p. and mixed m. p. 130—131°. Gum, crystals, and authentic material had identical infrared spectra in chloroform.

In another experiment, 6a,12a-dehydrorotenol acetate (500 mg.) was hydrogenated over 5% palladised charcoal (500 mg.) in ethyl acetate (20 ml.). Working up gave a gum which crystallised to give *6′,7′-dihydro-1′,5′-secorotenol acetate* (XV—XVIg) (26 mg.), m. p. 162—163° (Found: C, 68·15; H, 6·95. $C_{25}H_{30}O_7$ requires C, 67·85; H, 6·83%), $\nu_{max.}$ (mull) 1744 (OAc), 1680 (C=O) cm.$^{-1}$.

Acid-treatment of 6a,12a-*Dehydrorotenol, its Acetate, and* 6a,12a-*Isodehydrorotenol Acetate.*—6a,12a-Dehydrorotenol (300 mg.) was refluxed with 10% methanolic sulphuric acid (25 ml.) for 40 min. The blue solution was poured into water and extracted with ether. The extracts were washed with sodium hydrogen carbonate solution and water. Drying, evaporation, and chromatography from benzene on alumina (K3) gave the powdery mixture of 5′β-diastereoisomers of the spiro-compound (XVIIIa); identity with the specimen above was confirmed by the infrared (mull) spectrum, and crystallisation to give the diastereoisomer, m. p. and mixed m. p. 119—121°. 6a,12a-Dehydrorotenol acetate under similar conditions gave the same diastereoisomeric mixture (infrared) and the diastereoisomer, m. p. and mixed m. p. 119—121°.

6a,12a-Isodehydrorotenol acetate (700 mg.) similarly gave, after 60 minutes' refluxing, the racemic spiro-compound of the isorotenone series (cf. XVIII) (260 mg.), m. p. and mixed m. p. 126° (correct infrared spectrum).

Treatment of 6a,12a-*Dehydrorotenol with Sodium Acetate.*—The dehydro-compound (150 mg.) was refluxed for 2½ hr. with ethanol (8 ml.) saturated with sodium acetate, and then poured into water. The solid was filtered off, washed with a little methanol, and dried (150 mg.; m. p. 98—110°); the infrared spectrum (mull) was almost identical with that of mutarotenone.

Treatment of 6a,12a-*Dehydrorotenol Acetate and* 6a,12a-*Dehydroisorotenol Acetate with Aqueous Pyridine.*—(*a*) 6a,12a-Dehydroisorotenol acetate (300 mg.) was refluxed with pyridine (9 ml.) and water (2 ml.) for 30 min. The mixture was cooled, poured into dilute hydrochloric acid, and extracted with ether. The extract was washed, dried, and evaporated, and the residue crystallised from methanol, to give (±)-isorotenone, m. p. 166—169° (140 mg.) (correct infrared mull spectrum).

(*b*) 6a,12a-Dehydrorotenol acetate (300 mg.) was similarly refluxed for 90 min. Working up gave a glass (220 mg.) which on chromatography (alumina K1) from benzene gave 6a,12a-racemised rotenone (35 mg.), m. p. 110°. The infrared solution spectra of the glass and crystals were closely similar to that of rotenone.

Hydrolysis of 6a,12a-*Dehydrorotenol Acetate with Alcoholic Potassium Hydroxide.*—The acetate (500 mg.) was heated under reflux for 20 min. with N-alcoholic potassium hydroxide (15 ml.), and the red solution was acidified with dilute acetic acid and extracted with ether. The ethereal extract was washed, dried, and evaporated to a foamy resin that was chromatographed from benzene on alumina. The Durham test on the gummy product was positive but storage in methanol afforded the pale yellow 6,6a-dehydrorotenol (mixture of 5′β,12a-diastereoisomers) (20 mg.; Durham test negative), m. p. 128—129° (Found: C, 70·15; H, 5·75. Calc. for $C_{23}H_{22}O_6$: C, 70·05; H, 5·6%), $[\alpha]_D^{23·5}$ −96° (*c* 1·09), $\lambda_{max.}$ 242 (4·11) and 297 (4·34) mμ, $\nu_{max.}$ (mull) 1650i, 1640, 1620i, 1608, 1595 cm.$^{-1}$. The substance gave a red ferric reaction. A second experiment gave the diastereoisomers, m. p. 120—121°, which had identical infrared characteristics (chloroform) with the mixture above.

XUM

(+)- *and* (−)-6,6a-*Dehydro*-5′β-*rotenol*.—Rotenone (20 g.) was refluxed under nitrogen with 2N-potassium hydroxide (500 ml.). The solution became red and after 5 min. was poured into acetic acid (60 ml.) in water (2·5 l.). The mixture was extracted with ether, and the extracts were combined and shaken with charcoal, magnesium carbonate, and magnesium sulphate for 1 hr. After filtration, the solution was evaporated and the yellow gum was dissolved in a minimum of hot methanol. Crystallisation gave a diastereoisomeric mixture of 6,6a-dehydro-5′β-rotenols (6·5 g.), m. p. 105—110°. This was resolved by crystallisations from methanol, to give (+)-6,6a-*dehydro*-5′β-*rotenol*, m. p. 150—151° (Found: C, 70·3; H, 5·8%), $[\alpha]_D^{20}$ +203° (*c* 2), $\lambda_{max.}$ 244 (4·14), and 296 (4·36) mμ, $\nu_{max.}$ 1656i, 1637, 1621i, 1603, and 1555 cm.$^{-1}$, and (−)-6,6a-*dehydro*-5′β-*rotenol*, m. p. 122—123° (Found: C, 69·75; H, 5·5%), $[\alpha]_D^{20}$ −235° (*c* 2). The solution infrared spectrum of the latter was identical with that of the former. The mixture of diastereoisomers (5 g.) could also be obtained by adding 20% ethanolic potassium hydroxide (100 ml.) to rotenone (20 g.) in boiling ethanol (500 ml.), refluxing the mixture for 5 min., acidifying it with concentrated hydrochloric acid, and working it up as before.

Racemic 6,6a-*Dehydroisorotenol*.—(−)-Isorotenone (5 g.) was treated as above (second method), to give (±)-6,6a-*dehydroisorotenol* (0·35 g.), colourless needles (from methanol), m. p. 112° (Found: C, 69·65; H, 5·6. $C_{23}H_{22}O_6$ requires C, 70·05; H, 5·6%), $\nu_{max.}$ 1656i, 1629, 1595 cm.$^{-1}$.

Hydrogenation of (+)- *and* (−)-6,6a-*Dehydro*-5′β-*rotenol*.—The (+)-compound (100 mg.) in ethyl acetate (15 ml.) was hydrogenated over palladium–barium sulphate (2 mol. absorbed). Working up gave 6′,7′-dihydrorotenol, m. p. 135—136° (Found: C, 69·7; H, 6·75. Calc. for $C_{23}H_{26}O_6$: C, 69·35; H, 6·6%), $[\alpha]_D^{20}$ −196° (*c* 0·9) {whole unpurified product, $[\alpha]_D^{17}$ −187° (*c* 0·5)}. The m. p. was not depressed on admixture with the (−)-6′,7′-dihydro-5′β-rotenol (above), and the infrared spectra were the same. The product (25 mg.) was boiled for 3 hr. in ethanol (2 ml.) saturated with sodium acetate, and gave " ordinary " 6′,7′-dihydrorotenol (diastereoisomers), m. p. and mixed m. p. 129—130°, $[\alpha]_D^{20}$ −95° (*c* 0·9).

Similarly hydrogenated, (−)-6,6a-dehydro-5′β-rotenol gave 6′,7′-dihydrorotenol, m. p. 120—123°, $[\alpha]_D^{19}$ −86° (*c* 0·6); the infrared solution spectrum was the same as that of " ordinary " 6′,7′-dihydrorotenol. Racemisation and purification were completed as above, to give " ordinary " 6′,7′-dihydrorotenol, m. p. and mixed m. p. 130°, $[\alpha]_D^{20}$ −89° (*c* 1·2).

Acetylation of 6,6a-*Dehydrorotenol*.—The mixture of 5′β,12a-epimers (300 mg.), pyridine (3 ml.), and acetic anhydride (4 ml.) was kept at 20° for 16 hr. Working up and chromatography from chloroform–benzene (1 : 1) on alumina (K1) gave the *acetate*, m. p. 139° (from methanol) (Found: C, 69·05; H, 5·75. $C_{25}H_{24}O_7$ requires C, 68·8; H, 5·55%), $[\alpha]_D^{18}$ −70·2° (*c* 1·75), $\lambda_{max.}$ 335 (4·22) mμ and plateau-like peak 235—280 (4·05) mμ, $\lambda_{max.}$ (in $CHCl_3$) 1748 (OAc), 1650 (C=O). Acetylation of the (+)-5′β-epimer gave the acetate, m. p. 139—140°, $[\alpha]_D^{18}$ −73° (*c* 1), and that of the (−)-5′β-epimer gave material of m. p. 139—140°, $[\alpha]_D^{18}$ −72·5° (*c* 2·1), showing that racemisation occurs at position 12a. The acetate depressed the m. p. of 6a,12a-dehydro-5′β-rotenol acetate (m. p. 138—139°) to 120°. Hydrogenation of the acetate in ethyl acetate over palladium–barium sulphate gave a powdery product, the infrared spectrum of which (solution) was identical with that of dihydrorotenol acetate (above). The infrared band at 903 cm.$^{-1}$ (vinyl) disappears on hydrogenation.

Treatment of (±)-6,6a-*Isodehydrorotenol with Potassium Carbonate*.—(±)-6,6a-Isodehydrorotenol (300 mg.) was refluxed with acetone (10 ml.) containing an excess of potassium carbonate for 8 hr. Working up and chromatography from benzene on alumina (N3) gave (±)-isorotenone (120 mg.), m. p. and mixed m. p. 170°.

Treatment of (±)-6,6a-*Dehydrorotenol with Sodium Acetate*.—6,6a-Dehydrorotenol (5′β,12a-epimers, m. p. 121—124°) (300 mg.) was refluxed for 3 hr. with ethanol (30 ml.) saturated with sodium acetate. The product had m. p. 112—117°, and infrared measurement ($CHCl_3$) showed it to be virtually unchanged dehydrorotenol. (+)-6,6a-Dehydro-5′β-rotenol, similarly treated for 10 hr., gave mainly unchanged but 12a-racemised material, m. p. 118° to 144°, $[\alpha]_D^{19}$ −55° (*c* 1·4) (infrared identification); (−)-6,6a-dehydro-5′β-rotenol behaved similarly (10 hours' refluxing), the product having m. p. 118—144°, $[\alpha]_D^{19}$ −62° (*c* 1·9), with infrared characteristics as above.

Oximes and Iso-oximes of Rotenoids.—Rotenone α-oxime crystallised from ethanol in needles, m. p. 237°, $\lambda_{max.}$ 235 (4·36), 282 (4·24), 300 (4·06), and 312 (3·90) mμ, $\nu_{max.}$ (CaF_2, CCl_4; $<\sim$0·005M) 3592 cm.$^{-1}$, $\nu_{max.}$ (NaCl, $CHCl_3$; $\sim$0·04M) 1650i, 1613, 1600i, and 1502 cm.$^{-1}$ with a broad band near 3226 cm.$^{-1}$ (intermolecularly bonded OH). Rotenone β-oxime, needles, m. p. 249°, had

infrared data identical with that above, confirming its polymorphic nature [lit.,[23] α-form, m. p. 237°; β-form, m. p. 249° (stable)]. The β-oxime was unchanged by refluxing 5% ethanolic sodium hydroxide (5 hr.) and had $\nu_{max.}$ (NaCl, $CHCl_3$; ~0·04M) 3591 cm.$^{-1}$. Rotenone iso-oxime crystallised from acetone–ethanol after chromatographic purification, and had m. p. 210—211° (lit.,[6] m. p. 208° or 230°) (Found: C, 67·5; H, 5·8. Calc. for $C_{23}H_{23}NO_6$: C, 67·5; H, 5·6%), $\lambda_{max.}$ 287 (4·17) mμ, $\nu_{max.}$ (CaF_2, CCl_4; <~0·005M) 3162b and 3081b cm.$^{-1}$, $\nu_{max.}$ (NaCl, $CHCl_3$; ~0·04M) 3175b, 3058b, 1637, 1610, and 1502 cm.$^{-1}$. The compound gave a strong brown-purple ferric reaction.

(±)-Isorotenone oxime formed needles, m. p. 218° (decomp.) (lit.,[24] m. p. 230°) (Found: C, 67·7; H, 5·6; N, 3·2. Calc. for $C_{23}H_{23}NO_6$: C, 67·5; H, 5·6; N, 3·4%), $\lambda_{max.}$ 242 (4·70), 247 (4·67), 278 (3·93), 310 (3·45), and 322 (3·40) mμ, $\nu_{max.}$ (CaF_2, CCl_4; <~0·005M) 3593 cm.$^{-1}$, $\nu_{max.}$ (NaCl, $CHCl_3$) ~0·04M) 3610 (free OH), 3257 (intermolecularly bonded OH), 1621, 1587, and 1502 cm.$^{-1}$. (±)-Isorotenone iso-oxime, m. p. 191—192° (lit.,[25] m. p. 192°) (Found: C, 67·4; H, 5·65%), had $\nu_{max.}$ (CaF_2, CCl_4; <~0·005M) 3168b and 3088b cm.$^{-1}$, and gave a strong purple-black ferric reaction.

Dihydrorotenone oxime crystallised from chloroform–carbon tetrachloride in needles, m. p. 259°, $\lambda_{max.}$ 235 (4·27), 242i (4·13), 283 (4·18), 302 (3·97), and 315 (3·83) mμ, $\nu_{max.}$ (CaF_2, CCl_4; <~0·005M) 3592 cm.$^{-1}$, $\nu_{max.}$ (NaCl, $CHCl_3$; ~0·04M) 3597 (free OH) and 3311 (intermolecularly bonded OH), 1626i, 1616, 1597, and 1499 cm.$^{-1}$. The same compound was made by hydrogenating rotenone β-oxime over Adams catalyst in acetone. It was recovered unchanged when treated with concentrated hydrochloric acid for 64 hr.

α-Tetralone oxime formed prisms (from methanol), m. p. 104°, $\nu_{max.}$ (CaF_2, CCl_4, <~0·005M) 3595 cm.$^{-1}$. Cyclohexanone oxime had m. p. 90°, $\nu_{max.}$ (CaF_2, CCl_4, <~0·005M) 3602 cm.$^{-1}$.

(±)-12a-*Hydroxytoxicarol and its Acetate*.—(±)-Diacetyltoxicarol [26] (350 mg.) in acetic acid (10 ml.) was treated with 10% sodium dichromate in acetic acid (2 ml.) for 24 hr. at 20° and then poured into water and filtered. The solid, crystallised from aqueous acetic acid, had m. p. 180—182° (110 mg.), raised by crystallisation from methanol to m. p. 185° (lit.,[26] m. p. 184°). In neutral ethanol this (±)-12a-hydroxytoxicarol 11-acetate had $\lambda_{max.}$ 270 (4·50) mμ. In 0·01N-ethanolic potassium hydroxide the value was 270 (4·44) mμ after 1 min., but after 10 min. the peak had shifted to 280 (4·56) mμ.

(±)-12a-Hydroxytoxicarol 11-acetate (50 mg.) was refluxed with 10% ethanolic potassium hydroxide (1 ml.) for 15 min. The product, crystallised from hot aqueous acetic acid, had m. p. 219° (40 mg.), raised by crystallisation from methanol to 224° (lit.,[26] 226—227°). In neutral ethanol (±)-12a-hydroxytoxicarol had $\lambda_{max.}$ 273 (4·47) mμ, and in 0·01N-ethanolic potassium hydroxide 283 (4·59) mμ. In (±)-toxicarol the main band in ethanol was at 274 (4·61) mμ, shifted to 282 (4·56) mμ in 0·01N-ethanolic potassium hydroxide.

Behaviour of (−)-α-*Toxicarol in Alkaline Solution*.—The natural ketone [(−) in benzene] had $[\alpha]_D^{15}$ +84·3° (*c* 0·52 in acetone containing 28% of water). (−)-α-Toxicarol (*c* 0·56) in acetone (with 28% of water) containing 1·9% of potassium carbonate had: $[\alpha]_D^{15}$ +208°, +63·6°, +35·2°, 0° (after 5, 90, 210, and 1140 min.). (−)-α-Toxicarol had $[\alpha]_D^{15}$ +110° (*c* 0·24 in ethanol). The following rotations were observed for (−)-α-toxicarol (*c* 0·22) in ethanol containing 1% of sodium acetate: $[\alpha]_D^{15}$ +104°, +99° (after 10 and 420 min.). (−)-α-Toxicarol in ethanol containing 10% of water had $\lambda_{max.}$ 232 (4·19), 272 (4·55), and 295 (4·14) mμ. In the same solvent containing 2% of sodium acetate the values were 232 (4·25), 272 (4·53), and 295 (4·11) mμ (read after 30 min.).

Oxidation of the Hydroxy-compound (XXXIXa) *by Manganese Dioxide*.—Rotenone was reduced with lithium aluminium hydride in tetrahydrofuran, and the amorphous product (no C=O absorption, strong OH band; no Durham test) was used. The hydroxy-compound (1 g.) in acetone (50 ml.) was shaken with active manganese dioxide (20 g.) for 3 hr. After filtration and washing of the manganese dioxide with acetone, the acetone solution gave a solid (950 mg.) which crystallised from ethanol, to give 6a,12a-dehydrorotenone (60 mg.), m. p. and mixed m. p. 226—228°, then rotenone (total 446 mg.). Identity was confirmed by mixed m. p.s and the blue Durham reaction.

[23] Harper, *J.*, 1939, 1424.
[24] Takei, *Ber.*, 1928, **61**, 1003.
[25] Takei, Miyajima, and Ono, *Ber.*, 1931, **64**, 1000.
[26] Clark, *J. Amer. Chem. Soc.*, 1934, **56**, 987.

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Dehydrogenation of Natural Rotenone and (−)-*Isorotenone with Manganese Dioxide.*—(−)-Isorotenone (1 g.) was shaken at 20° with active manganese dioxide (10 g.) and acetone (50 ml.) for 12 hr. Working up as above and crystallisation from chloroform–methanol gave 6a,12a-dehydroisorotenone (784 mg.), m. p. and mixed m. p. 194—195°, $\nu_{max.}$ ($CHCl_3$), 1634 (aryl conj. α-unsatd. ketone), 1613, 1582, and 1502 cm.$^{-1}$. (−)-Isorotenone (10 g.) was refluxed with active manganese dioxide (50 g.) in acetone (250 ml.) and gave 6a,12a-dehydroisorotenone (7·5 g.), m. p. 195—196°.

Rotenone (2 g.) was shaken for 5 days at 20° with active manganese dioxide (10 g.) in acetone. Working up gave 6a,12a-dehydrorotenone (1·34 g.), m. p. and mixed m. p. 223—224° (from chloroform–methanol), $\nu_{max.}$ ($CHCl_3$) 1634 cm.$^{-1}$ (C=O). Rotenone (1 g.), when refluxed with acetone (30 ml.) containing active manganese dioxide (5 g.) for 3 hr., gave 6a,12a-dehydrorotenone (0·68 g.), m. p. and mixed m. p. 224°.

Oxidation of α- *and* β-*Toxicarol with Manganese Dioxide.*—(−)-α-Toxicarol (100 mg.) was shaken with active manganese dioxide (1 g.) in acetone for 7 hr. The solid was filtered off and washed with chloroform. The filtrate and washings were diluted with methanol, and the precipitate was collected and crystallised from chloroform and methanol, to give the orange lactone (XLIId; R = OH) (29 mg.), m. p. 290—291° (decomp.) (Found: C, 65·25; H, 4·3. Calc. for $C_{23}H_{18}O_8$: C, 65·4; H, 4·3%), $\nu_{max.}$ (mull) 1742 (lactone) and 1650 (chelated ketone) cm.$^{-1}$ (lit.,[14] m. p. 283—284°). (±)-β-Toxicarol (100 mg.) similarly gave the corresponding compound in the β-series [cf. (XXXII)] (55 mg.), orange needles, m. p. 298—299° (decomp.) (Found: C, 65·45; H, 4·45%), $\nu_{max.}$ (mull) 1748 and 1653 cm.$^{-1}$.

Oxidation of 6a,12a-*Dehydrorotenone with Lead Tetra-acetate.*—Dehydrorotenone (1·4 g.) in glacial acetic acid (50 ml.) was shaken with lead tetra-acetate (5 g.) for 7 days. Water (50 ml.) was added and the precipitate was filtered off, washed with methanol, and extracted with boiling chloroform. The chloroform extract was concentrated and methanol was added. The precipitate was collected and, after crystallisation from chloroform–methanol, gave rotenonone (1·05 g.), yellow plates, m. p. and mixed m. p. 295—297° (decomp.) (Found: C, 67·75; H, 4·55. Calc. for $C_{23}H_{16}O_7$: C, 68·0; H, 4·45%), $\lambda_{max.}$ (in $CHCl_3$) 265 (4·40), 298 (4·33), and 345 (3·95) mμ, $\nu_{max.}$ 1730 (lactone), 1645 (unsatd. ketone), 1620, 1596, 1557, and 1502 (aryl) cm.$^{-1}$.

Two of us (P. J. G. and D. A. W.) are grateful for D.S.I.R. postgraduate awards, and one of us (P. J. G.) thanks Shell Research Ltd. for a post-doctorate award. We thank Messrs. Cooper, McDougall, and Robertson for gifts of timbo resin.

University of London, King's College,
Strand, London, W.C.2.
Imperial College of Science and Technology,
South Kensington, London, S.W.7.

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556. *The Synthesis of Thyroxine and Related Compounds. Part XVII.*[1] *The Preparation of Some Additional Compounds related to Thyroxine.*

By A. Dibbo, J. C. P. Sly, L. Stephenson, T. Walker, W. K. Warburton, and K. D. E. Whiting.

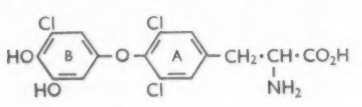
3,5,3′-Trichloro-5′-hydroxy-D- and -L-thyronine (I) have been prepared by the pyridinium salt method. 4-*p*-Hydroxyphenoxy-3,5-di-iodoacetophenone (III) has been prepared from 3,5-di-iodo-4-*p*-methoxyphenoxycinnamic acid. 2-(4-*p*-Hydroxyphenoxy-3,5-di-iodophenyl)ethanol (IV) has been prepared from the corresponding phenylacetic acid.

3,5-Di-iodo-*NN*-dimethyl-D-thyronine has been prepared by a modification of Elks and Waller's method.[2] Some diphenyl sulphides [*e.g.*, (VIII)] related to D-thyronine have been prepared by the pyridinium salt method, and some biphenyls have been obtained from 4-hydroxy-3,5-dinitrobenzoic acid and converted into derivatives of phenylacetic acid [*e.g.*, (XI)].

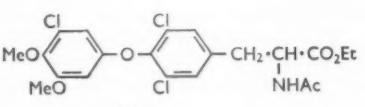
Several substituted D- and L-thyronines and some carboxylic acids related to thyroxine are described.

During the past three years we have prepared many compounds related to thyroxine for testing as depressants of blood cholesterol. We now report the preparation of several of these compounds. We have been interested particularly in derivatives of D-phenylalanine, for in many instances such compounds have a greater effect on fat and steroid metabolism than would have been expected from their action on the heart and on basal metabolic rate.[3]

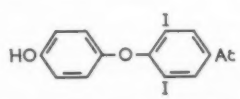
3,5,3′-Trichloro-5′-hydroxy-D- and -L-thyronine (I) were prepared by the pyridinium salt method [4] from 6-chloro-4-hydroxyveratrole and *N*-acetyl-3,5-dinitro-D- and -L-tyrosine ethyl ester. The phenol was obtained from 5-chloroveratraldehyde *O*-acetyloxime: conversion into the nitrile, then hydrolysis, hypobromite degradation, diazotization, and decomposition of the diazonium salt with aqueous sulphuric acid gave the phenol in 30% overall yield (9% from vanillin). *N*-Acetyl-4-(3-chloro-4,5-dimethoxyphenoxy)-3,5-dinitrophenylalanine ethyl ester was reduced by hydrogen in the presence of platinum to the diamine (reduction in the presence of palladium caused loss of chlorine), which was tetrazotized and converted into the trichloro-compound (II). Acid-hydrolysis of this and demethylation of the amino-acid gave the thyronine (I), but special precautions against oxidation had to be taken while the amino-acid was in solution. Treating the ester (II) with hydriodic acid gave a much lower yield of the thyronine.



(I)



(II)



(III)

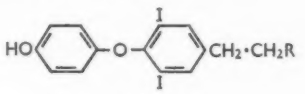
3,5,3′-Trichloro-5′-hydroxy-L-thyronine has little if any thyroactivity,[5] although 3,5,3′-trichloro-L-thyronine is demonstrably active.[6] It has been suggested that normal thyroactivity is due to an *o*-quinonoid compound derived initially from 3,5,3′-tri-iodo-L-thyronine

[1] Part XVI, *J.*, 1961, 2651.
[2] Elks and Waller, *J.*, 1952, 2366.
[3] (*a*) Boyd and Oliver, *J. Endocrinol.*, 1960, **21**, 25, **33**; (*b*) Cuthbertson, Elcoate, Ireland, Mills, and Shearley, *ibid.*, pp. 45, 69.
[4] Chalmers, Dickson, Elks, and Hems, *J.*, 1949, 3424.
[5] Boyd, unpublished results.
[6] Cuthbertson, Elcoate, Ireland, Mills, and Shearley, unpublished results.

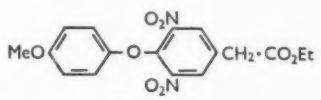
by 5′-hydroxylation (the postulated tri-iodocatechol has not yet been obtained, although 3′-hydroxy-3,5-di-iodo-L-thyronine has now been prepared [7]). The low activity of 3,5,3′-trichloro-5′-hydroxy-L-thyronine does not support the hydroxylation theory.

Cookson and Green [8] obtained the oxime of 3,5-di-iodo-4-*p*-methoxyphenoxyacetophenone as a by-product from the preparation of β-thyroxine. We have improved the preparation of this oxime and converted it into the hydroxy-ketone (III) by successive treatment with hydrochloric and hydriodic acid.

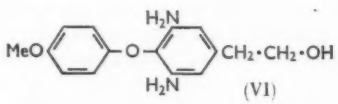
2-(4-*p*-Hydroxyphenoxy-3,5-di-iodophenyl)ethanol (IV) was prepared from ethyl 3,5-dinitrophenyl-4-methoxyphenoxyacetate (V). Reduction of the ester, first with hydrogen and then with lithium aluminium hydride, gave the diamino-alcohol (VI), which was tetrazotized; the tetrazonium salt was then treated with iodine. Acetylation of the resulting di-iodo-alcohol to facilitate chromatographic separation, then treatment with hydriodic acid, gave the substituted alkyl iodide (VII), and hydrolysis with sodium carbonate gave the alcohol (IV).



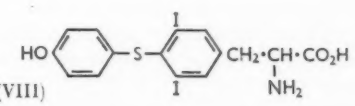
(IV: R = OH)
(VII: R = I)



(V)

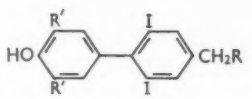


(VI)



(VIII)

The metabolic rôle of the amino-group in iodinated thyronines is still not clear; [9] we therefore prepared 3,5-di-iodo-*NN*-dimethyl-D-thyronine. The selective *N*-methylation of 3,5-di-iodo-D-thyronine was not attempted. Total methylation with diazomethane and subsequent hydrolysis of the methoxy-group were unsuccessful, but treating α-bromo-β-(4-hydroxy-3,5-dinitrophenyl)propionic acid [2] with dimethylamine gave a dimethylamino-acid that we assume, from its mode of formation and optical activity, to be of the D-series. The amino-acid was esterified and converted by known methods [4] into 3,5-di-iodo-*NN*-dimethyl-D-thyronine, but during the tetrazotization and introduction of iodine much of the product was lost in the acid medium (in the synthesis of di-iodothyronine the corresponding amino-group is already acetylated). The dimethylamino-acid has little or no thyroactivity.[6]



[IX: R = CH(NH$_2$)·CO$_2$H; R′ = I]
(X: R = Cl; R′ = H)
(XI: R = CO$_2$H; R′ = H)

We prepared ethyl 3,5-dinitro-4-phenylthiophenylacetate in 60% yield by treating the pyridinium salt derived from ethyl 4-hydroxy-3,5-dinitrophenylacetate with benzenethiol. The same diphenyl sulphide was obtained, but only in 24% yield, by treating ethyl 4-chloro-3,5-dinitrophenylacetate with benzenethiol in alcoholic potassium hydroxide. The nitro-groups were catalytically reduced with hydrogen, despite the presence of sulphur in the molecule, and from the diamine we obtained 3,5-di-iodo-4-phenylthiophenylacetic acid in reasonable overall yield. The way was therefore clear for making the sulphur analogue (VIII) of 3,5-di-iodo-D-thyronine; it was indeed obtained, although the final demethylation

[7] Doskotch and Lardy, *J. Amer. Chem. Soc.*, 1958, **80**, 6230.
[8] Cookson and Green, *J.*, 1952, 827.
[9] Pitt-Rivers and Tata, "The Thyroid Hormones," Pergamon Press, London, 1959, p. 156.

XUM

gave only a 51% yield. The corresponding tri- and tetra-iodo-compounds were also prepared. Harington [10] made the DL-di- and tetra-iodo-compounds from *p*-methoxybenzenethiol and 3,4,5-tri-iodo-1-nitrobenzene by the acetamidomalonic ester method.

The biphenyl (IX) corresponding to DL-thyroxine was prepared by Barnes, Cookson, Dickson, Elks, and Poole [11] from 3,5-di-iodo-4-*p*-methoxyphenylbenzyl chloride (X); the benzyl chloride was made by treating the corresponding alcohol with thionyl chloride and was not isolated. We have obtained the pure benzyl chloride in 71% yield by treating the same alcohol with phosphorus pentachloride and have converted it into 3,5-di-iodophenyl-4-*p*-hydroxyphenylacetic acid (XI). The benzyl chloride, when treated with potassium cyanide, gave a nitrile that was converted into the demethylated phenylacetic acid by hydriodic acid. The corresponding dichloro-acid was prepared similarly; the di-iodo-acid was also converted into the tri- and the tetra-iodo-acid.

We were not able to obtain methyl 3,5-dinitrophenyl-4-*p*-methoxyphenylacetate by treating *p*-iodoanisole with methyl 4-chloro-3,5-dinitrophenylacetate, nor were we able to lengthen the side-chain of the corresponding benzoic acid by the Arndt–Eistert method.

We prepared 3,5-di-iodo-4-isopropoxyphenylacetic acid, a compound that contains a large part of the *p*-phenoxyphenylacetic acid skeleton, in order to establish whether or not the whole biphenyl ether system was essential. The compound, prepared by treating the hydroxy-acid with isopropyl bromide, proved to be inactive.

3,5-Di-iodo-3′,5′-dimethylthyronine is probably resistant to changes in oxidation state at the 3′- and the 5′-position. The L- and the DL-compound have been described.[11,12] We have now prepared the D-isomer. Our yields in the later stages (unlike those reported earlier) were particularly good, probably because we worked on a larger scale and so were able to carry out the critical tetrazotization and Sandmeyer reactions without excessive dilution.

Almost all the compounds that have been tested for thyroactivity contain a 4-hydroxy-group in ring B. We prepared 3,5-di-iodo-4-phenoxy-D-phenylalanine, a compound in which this group is absent, by the pyridinium salt method, but using phenol instead of *p*-methoxyphenol. The compound is effective in lowering blood cholesterol.[6]

3,5-Dichloro-4-(3-chloro-4-hydroxyphenoxy)benzoic acid and the corresponding 3,5,3′-tri-iodo-compound were prepared by partial halogenation of the dichloro- and di-iodo-compounds. 3,5-Dibromo-4-(*p*-hydroxyphenoxy)phenylacetic acid was prepared by the pyridinium salt method and converted into the tri- and tetra-bromo-compounds; similarly prepared were the corresponding tri- and tetra-chloro-acids and also 3,5-di-iodo-4-phenoxyphenylacetic acid.

An extensive study has been made in these laboratories of the effect on blood cholesterol of halogenated thyronines, particularly in the D-series. The nineteen D-thyronines and six L-thyronines shown in the Table have been prepared; some of these are already known in the DL-form. An account of some biological effects of the compounds described in this and earlier papers will be submitted for publication elsewhere.[6]

Series	Substituents				Series	Substituents			
	3	5	3′	5′		3	5	3′	5′
D and L	Cl	Cl	Cl	H	D and L	Br	Br	Br	H
D and L	Cl	Cl	Cl	Cl	D and L	Br	Br	Br	Br
D	Cl	Cl	Cl	I	D	Br	Br	Br	I
D	Cl	Cl	Br	H	D	Br	Br	I	H
D	Cl	Cl	Br	Br	D	Br	Br	I	I
D	Cl	Cl	I	H	D	I	I	Cl	H
D	Cl	Cl	I	I	D	I	I	Cl	Cl
D and L	Cl	I	I	I	D	I	I	Br	H
D and L	Br	Br	H	H	D	I	I	Br	Br
D	Br	Br	Cl	H					

[10] Harington, *Biochem. J.*, 1948, **43**, 434.
[11] Barnes, Cookson, Dickson, Elks, and Poole, *J.*, 1953, 1448.
[12] Bruice, Kharasch, and Winzler, *J. Org. Chem.*, 1953, **18**, 83.

Experimental

M. p.s are corrected. Rotations, except where stated otherwise, refer to 1:1 (v/v) N-HCl–EtOH solutions (*c* 1). Chromatography was carried out as described earlier.[13] Presence of solvent of crystallization indicated in molecular formulæ was confirmed by infrared spectroscopy.

5-Chloroveratronitrile.—5-Chloroveratraldehyde[14] (50·1 g.) in warm absolute ethanol (100 ml.) was treated with a warm solution of hydroxylamine hydrochloride (21 g.) in water (25 ml.), then with a solution of sodium hydroxide (15 g.) in water (20 ml.), and the mixture was set aside for 2½ hr. Ice (130 g.) was added and the mixture saturated with carbon dioxide. The white solid was washed with water, drained nearly dry, and warmed with acetic anhydride (150 ml.) for 30 min. The solution was poured into cold water (400 ml.), and the precipitated white solid washed with water and recrystallized from ethanol, giving needles of *5-chloroveratronitrile* (39·0 g., 79%), m. p. 101—102·5°. A second crop (6·4 g., 13%), m. p. 99·5—100·5°, was obtained from the mother-liquors. Further crystallization from ethanol gave needles, m. p. 101·5—102·5° (Found: C, 54·5; H, 3·8; Cl, 18·2; N, 6·6. $C_9H_8ClNO_2$ requires C, 54·7; H, 4·1; Cl, 17·9; N, 7·1%).

5-Chloroveratramide.—5-Chloroveratronitrile (72·5 g.) was added to a stirred mixture of hydrogen peroxide (100-vol.; 390 ml.) and water (1·3 l.). Then 10N-sodium hydroxide (46 ml.) was added and the mixture was heated slowly to 80° and stirred at that temperature for about 20 min. After it had cooled, the white solid was filtered off. Recrystallization from aqueous ethanol gave the *amide* (64·0 g., 81%), m. p. 144—145°. Further crystallization from 30% ethanol gave needles, m. p. 144—145° (Found: C, 50·3; H, 4·8; Cl, 16·4; N, 6·4. $C_9H_{10}ClNO_3$ requires C, 50·1; H, 4·7; Cl, 16·4; N, 6·5%).

3-Chloro-4,5-dimethoxyaniline.—Bromine (49·7 g.) was added to a stirred solution of sodium hydroxide (75·5 g.) in water (475 ml.) containing crushed ice (300 g.). The foregoing amide (64·0 g.) was added, with stirring, and the mixture heated at 75° for 30 min., then a solution of sodium hydroxide (151 g.) in water (150 ml.) was added and the solution kept at 80—90° for 1 hr. The solid *amine* which separated on cooling recrystallized from aqueous ethanol giving brown needles (42·2 g., 76%), m. p. 96·5—97·5°. Two more recrystallizations from aqueous ethanol gave needles, m. p. 97—97·5° (Found: C, 51·7; H, 5·7; Cl, 18·9; N, 7·3. $C_8H_{10}ClNO_2$ requires C, 51·2; H, 5·4; Cl, 18·9; N, 7·5%).

3-Chloro-4,5-dimethoxyphenol.—The preceding amine (25·4 g.) was diazotized. The reaction mixture was stirred for 15 min. and the yellow suspension poured into a stirred, boiling mixture of concentrated sulphuric acid (94 ml.) and water (80 ml.). The whole was cooled and the dark red solid which separated was boiled with ethanol (charcoal), then the solution was filtered, diluted with a little water, and set aside overnight. A little dark red gum was filtered off and the filtrate evaporated to dryness under reduced pressure. The solid residue was stirred with a little benzene and dried, leaving material (11·7 g., 46%) of m. p. 150°. A sample recrystallized from carbon tetrachloride gave off-white needles of the *phenol*, m. p. 148—149° (Found: C, 51·0; H, 5·0; Cl, 18·8; OMe, 32·4. $C_8H_9ClO_3$ requires C, 50·1; H, 4·8; Cl, 18·8; OMe, 32·9%).

Ethyl Ester of N-Acetyl-4-(5-chloro-3,4-dimethoxyphenoxy)-3,5-dinitro-D- and -L-phenylalanine.—The ethyl ester of *N*-acetyl-3,5-dinitro-D-tyrosine (30·7 g.) was warmed for 30 min. on the steam-bath with toluene-*p*-sulphonyl chloride (19·1 g.) and dry pyridine (155 ml.). The phenol mentioned above (8·8 g.) was added and the mixture refluxed for 1½ hr., cooled, acidified with 2N-hydrochloric acid, and extracted with chloroform. The extracts were washed with water, 2N-sodium hydroxide, and water, then dried ($CaCl_2$). The chloroform was distilled off leaving a dark red oil which was passed, in acetone, through an alumina column. The orange-yellow solution obtained was evaporated to dryness, leaving a yellow solid which crystallized from ethanol as yellow needles (16·9 g., 71%), m. p. 156—157°. Further crystallization gave pale yellow needles of the *ester*, m. p. 157—157·5°, $[\alpha]_D^{19}$ −29·8° (*c* 0·87 in chloroform) (Found: C, 49·0; H, 4·3; Cl, 6·8; N, 8·0. $C_{21}H_{22}ClN_3O_{10}$ requires C, 49·3; H, 4·3; Cl, 6·9; N, 8·2%). The L-*isomer*, prepared similarly, had m. p. 157—158°, $[\alpha]_D^{22}$ +30·0° (Found: C, 49·0; H, 4·3; Cl, 7·3; N, 8·5%).

Ethyl Ester of N-Acetyl-3,5-diamino-4-(5-chloro-3,4-dimethoxyphenoxy)-D- and -L-phenylalanine.—The preceding D-compound (22·3 g.) was reduced in methanol (2 l.) with hydrogen in the presence of 5% platinum–carbon (4·5 g.). Removal of the methanol left crystals, a small

[13] Varcoe and Warburton, *J.*, 1960, 2711.
[14] Raiford and Parry, *J. Org. Chem.*, 1942, **7**, 354.

portion of which, recrystallized from aqueous methanol, gave the D-*diamine* as colourless needles, m. p. 104—105° (Found: C, 53·7; H, 6·1; Cl, 7·7; N, 8·7. $C_{21}H_{26}ClN_3O_6,H_2O$ requires C, 53·7; H, 6·0; Cl, 7·6; N, 8·9%). The corresponding L-diamine did not crystallize; its *diacetyl derivative* had m. p. 185—186° (Found: C, 55·7; H, 6·0; Cl, 6·8; N, 8·0. $C_{25}H_{30}ClNO_8$ requires C, 56·0; H, 5·6; Cl, 6·6; N, 7·8%).

Ethyl Ester of N-*Acetyl*-3,5-*dichloro*-4-(5-*chloro*-3,4-*dimethoxyphenoxy*)-D- *and* -L-*phenylalanine*.—The D-diamine (from 22·3 g. of the dinitro-compound) was tetrazotized, and the tetrazonium salt decomposed with cuprous chloride. The combined chloroform solutions were washed with water, 2N-sodium hydroxide, and water, dried ($MgSO_4$), evaporated to a small volume, and passed through a column of "Florisil." Evaporation of the eluate gave the D-trichloro-compound as an orange gum (15·1 g., 71%). The L-*trichloro-compound* was obtained in the same way, but with m. p. 140·5—141° (Found: C, 51·6; H, 4·7; Cl, 21·3; N, 2·7. $C_{21}H_{22}Cl_3NO_6$ requires C, 51·4; H, 4·5; Cl, 21·7; N, 2·8%).

3,5-*Dichloro*-4-(5-*chloro*-3,4-*dimethoxyphenoxy*)-D-*phenylalanine*.—The preceding crude D-ester (11·8 g.) was refluxed in acetic acid (60 ml.) and 5N-hydrochloric acid (120 ml.) for 2½ hr. A solid crystallized from the cooled solution and was collected. Its solution in pyridine was filtered and diluted at the b. p. with water. Crystals of 3,5-*dichloro*-4-(5-*chloro*-3,4-*dimethoxyphenoxy*)-D-*phenylalanine* separated (4·3 g.; m. p. 190—200°). A further 1·0 g. (total yield 50%) was obtained from the mother-liquors (Found: C, 45·9; H, 4·2; Cl, 24·1; N, 3·3. $C_{17}H_{16}Cl_3NO_5,H_2O$ requires C, 46·6; H, 4·1; Cl, 24·3; N, 3·2%).

3,5,3′-*Trichloro*-5′-*hydroxy*-D-*thyronine*.—The preceding compound (2·0 g.) was refluxed for 3 hr. with glacial acetic acid (40 ml.) and constant-boiling hydrobromic acid (40 ml.), and the solution was diluted with hot water (80 ml.), treated with charcoal, filtered, and brought to pH 4 with solid sodium carbonate. On cooling, 3,5,3′-*trichloro*-5′-*hydroxy*-D-*thyronine* crystallized as colourless needles (1·1 g., 59%), m. p. 204° (decomp.). Recrystallization from aqueous acetic acid gave needles, m. p. 215°. After drying at 155°/0·2 mm. this compound still contained some acetic acid (infrared) and was redissolved in 0·5N-hydrochloric acid and brought to pH 2 at the b. p. with N-sodium hydroxide, giving off-white needles, m. p. 222° (decomp.), $[\alpha]_D^{20}$ −28·2° (Found: C, 44·4; H, 3·1; Cl, 26·1. $C_{15}H_{12}Cl_3NO_5,H_2O$ requires C, 43·9; H, 3·4; Cl, 25·9%).

3,5,3′-*Trichloro*-5′-*hydroxy*-L-*thyronine*.—The ethyl ester of *N*-acetyl-3,5-dichloro-4-(5-chloro-3,4-dimethoxyphenoxy)-L-phenylalanine (1·8 g.) was refluxed for 4 hr. with acetic acid (18 ml.) and constant-boiling hydriodic acid (18 ml.). Removal of the acids under reduced pressure left a dark residue which was dissolved in water and treated with a little "Versene" and sodium hydrogen sulphite. The pH was adjusted to 4 with sodium acetate; a dark gum separated and later solidified. The solid was dissolved in 2N-hydrochloric acid, the solution boiled with charcoal and filtered, and the filtrate neutralized as before. The dark solid was redissolved in hydrochloric acid, and the solution again treated with "Versene" and sodium hydrogen sulphite, then neutralized. 3,5,3′-Trichloro-5′-hydroxy-L-thyronine was obtained as a dark grey solid (450 mg., 31%), m. p. 221—223° (decomp.) (Found: C, 45·7; H, 3·5; Cl, 24·4; N, 3·4. Calc. for $C_{15}H_{12}Cl_3NO_5$: C, 45·9; H, 3·1; Cl, 27·1; N, 3·6%). This compound, which was not quite pure, had an infrared spectrum similar to that of the D-compound, but its rotation could not be determined.

3,5-*Di-iodo*-4-p-*methoxyphenoxyacetophenone Oxime* (with Dr. A. C. RITCHIE).—Hydroxylamine hydrochloride (10·25 g.) in water (19·6 ml.) was added to a solution of sodium (3·36 g.) in ethanol (280 ml.). The precipitated sodium chloride was filtered off, and 3,5-di-iodo-4-*p*-methoxyphenoxycinnamic acid [8] (35 g.) added, then dioxan (84 ml.). The mixture was refluxed for 24 hr., then cooled, and the precipitate washed with water and alcohol, then dried at 60°, giving β-amino-β-(3,5-di-iodo-4-*p*-methoxyphenoxyphenyl)propionic acid (8·63 g., 24%), m. p. 230—232° (decomp.). The yellow filtrate from the reaction with hydroxylamine was concentrated under reduced pressure. Water (1·5 l.) was added and the mixture heated on the steam-bath under reduced pressure until all the alcohol had been removed. Filtration gave a pale yellow solid (24·7 g.), m. p. 156—160° (decomp.). This material, dissolved in benzene containing 5% of dioxan, was passed through a column of alumina and eluted with benzene containing 20% of ethanol. Evaporation of the eluate left a brown solid (14 g.). This crystallized from methanol (charcoal), giving almost colourless needles of 3,5-di-iodo-4-*p*-methoxyphenoxyacetophenone oxime (10·23 g., 36·5%), m. p. 180—182°. Cookson and Green [8] report m. p. 179—181°.

3,5-*Di-iodo*-4-p-*methoxyphenoxyacetophenone* (with Dr. A. C. RITCHIE).—The preceding

compound (12 g.) was refluxed with ethanol (120 ml.) and 10N-hydrochloric acid (24 ml.) for 1 hr. and the mixture cooled to room temperature, then refrigerated for 2½ hr. The solid was collected and washed with methanol, then with water until neutral, leaving the ketone (9·38 g., 81%), m. p. 138—143°. Cookson and Green [8] report m. p. 141—142°.

4-p-*Hydroxyphenoxy*-3,5-*di-iodoacetophenone* (with Dr. A. C. RITCHIE).—The preceding compound (9·25 g.) was refluxed in glacial acetic acid (36 ml.) and constant-boiling hydriodic acid (27 ml.) for 30 min., then cooled to room temperature and refrigerated for 1 hr. The yellow solid was collected, washed with a little acetic acid, then with water, and dissolved in methanol (170 ml.) containing a little benzene. Treatment with charcoal, filtration, and reduction of volume gave a solid, which was washed with methanol, leaving colourless 4-p-*hydroxyphenoxy*-3,5-*di-iodoacetophenone* (7·18 g.), m. p. 217—221° (Found: C, 34·7; H, 1·8; I, 51·9. $C_{14}H_{10}I_2O_3$ requires C, 35·0; H, 2·1; I, 52·8%).

3,5-*Di-iodo*-4-*isopropoxyphenylacetic Acid* (with Dr. A. C. RITCHIE).—4-Hydroxy-3,5-di-iodophenylacetic acid (9·95 g.) was dissolved in a solution of potassium hydroxide (12 g.) in water (48 ml.) and ethanol (100 ml.). Isopropyl bromide (40 ml.) was added and the mixture refluxed for 2 hr. Most of the ethanol was removed under reduced pressure and the solution diluted to about 400 ml. with water, extracted with ether, then acidified to pH 1. The oil which separated solidified in the refrigerator overnight and the solid was filtered off, washed well with water, then recrystallized from benzene and light petroleum (b. p. 60—80°) (charcoal), giving 3,5-*di-iodo*-4-*isopropoxyphenylacetic acid* (8·4 g., 76%), m. p. 129—133° (Found: C, 29·6; H, 2·75; I, 56·7. $C_{11}H_{12}I_2O_3$ requires C, 29·5; H, 2·7; I, 56·7%).

2-(3,5-*Diamino*-4-p-*methoxyphenoxyphenyl*)*ethanol*.—Ethyl 3,5-diamino-4-*p*-methoxyphenoxyphenyl acetate [15] (14 g.) was reduced in tetrahydrofuran with lithium aluminium hydride, giving the *alcohol* (8·5 g., 69%), m. p. 127·5—129° (from chloroform) (Found: C, 66·1; H, 6·7; N, 9·6. $C_{15}H_{18}N_2O_3$ requires C, 65·7; H, 6·6; N, 10·2%). The NN′-*diacetyl derivative* had m. p. 181—182·5° (Found: N, 7·5. $C_{19}H_{22}N_2O_5$ requires N, 7·8%).

3,5-*Di-iodo*-4-p-*methoxyphenoxyphenethyl Acetate*.—The preceding diamine (8·7 g.) was tetrazotized, and the tetrazonium salt decomposed with iodine in potassium iodide solution,[4] giving a gum, which was warmed for 1 hr. with acetic acid (50 ml.) and acetic anhydride (10 ml.). The cooled solution was poured into water and the *acetyl compound* separated (12·3 g., 72%; m. p. 95·5—98·5°) (Found: C, 38·5; H, 3·1; I, 47·4. $C_{17}H_{16}I_2O_4$ requires C, 37·9; H, 3·0; I, 47·2%).

4-p-*Hydroxyphenoxy*-3,5-*di-iodophenethyl Iodide*.—Demethylation of the preceding compound (12·3 g.) with hydriodic acid gave the *iodide* (11·8 g., 87%), m. p. 157·5—160·5° (Found: C, 28·8; H, 1·9; I, 64·5. $C_{14}H_{11}I_3O_3$ requires C, 28·4; H, 1·9; I, 64·3%).

4-p-*Hydroxyphenoxy*-3,5-*di-iodophenethyl Alcohol*.—The preceding compound was refluxed for 15 hr. with 10% sodium carbonate solution (150 ml.) and ethanol (190 ml.). The mixture was cooled and extracted three times with ether. The ether extracts were combined, washed with water, and dried (Na_2SO_4). Removal of the ether left an oil, which crystallized from benzene on addition of light petroleum (b. p. 40—60°). The *alcohol* (5·6 g., 69%) had m. p. 112—116° (Found: I, 53·7. $C_{14}H_{13}I_2O_3$ requires I, 52·7%).

NN-*Dimethyl*-3,5-*dinitro*-D-*tyrosine*.—α-Bromo-β-(4-hydroxy-3,5-dinitrophenyl)propionic acid [1] (10·0 g.) was dissolved in 25% (w/v) aqueous dimethylamine and left for 3 days. Most of the dimethylamine was then removed under reduced pressure and the solution cooled and made just acid with 2N-hydrochloric acid. The orange solid was dissolved in 0·4N-sodium hydroxide and the solution filtered, cooled, and brought to pH 4·5 with sodium acetate. NN-*Dimethyl*-3,5-*dinitro*-D-*tyrosine* separated as orange crystals (6·50 g., 73%), m. p. 250° (explodes) (Found: C, 43·6; H, 4·3; N, 13·8. $C_{11}H_{13}N_3O_7$ requires C, 44·1; H, 4·4; N, 14·0%).

The acid (41·0 g.) was refluxed for 6 hr. in ethanol while hydrogen chloride was passed in. The ethanol was removed and the residue dissolved in water (600 ml.) and ethanol (150 ml.). The solution was treated with charcoal and filtered, then neutralized with sodium acetate at the b. p. The *ethyl ester* separated as orange crystals (32·0 g., 76%), m. p. 193—197° (decomp.), $[\alpha]_D^{20}$ −72° (*c* 1 in dioxan containing 10% of 2N-hydrochloric acid) (Found: C, 46·9; H, 5·1; N, 12·2. $C_{13}H_{17}N_3O_7,\frac{1}{2}H_2O$ requires C, 46·5; H, 5·4; N, 12·5%).

Ethyl Ester of 4-p-*Methoxyphenoxy*-NN-*dimethyl*-3,5-*dinitro*-D-*phenylalanine*.—The preceding ester (5·00 g.) was warmed with toluene-*p*-sulphonyl chloride (3·26 g.) and pyridine (25 ml.) on the steam-bath for 30 min. *p*-Methoxyphenol (5·6 g.) was added and the mixture refluxed for

[15] Meltzer, Lustgarten, and Fischman, *J. Org. Chem.*, 1957, **22**, 1577.

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1 hr. After cooling, the solution was treated with 2N-hydrochloric acid, then extracted with chloroform several times. The chloroform extract was washed with water, dried ($MgSO_4$), and evaporated, leaving a residue which recrystallized from aqueous ethanol. The *diphenyl ether* separated as pale yellow needles (2·9 g., 44%), m. p. 87·5—89°, $[\alpha]_D^{20}$ −27° (*c* 1 in dioxan containing 10% of 2N-hydrochloric acid) (Found: C, 55·3; H, 5·0. $C_{20}H_{23}N_3O_8$ requires C, 55·4; H, 5·3%).

3,5,-*Di-iodo*-NN-*dimethyl*-D-*thyronine*.—The preceding compound (9·0 g.) was reduced in acetic acid (50 ml.) with hydrogen in the presence of 5% palladium–charcoal (1 g.), and the diamine solution tetrazotized and treated with iodine in potassium iodide.[4] The chloroform solutions were combined and washed with water containing sodium hydrogen sulphite, then dried ($MgSO_4$) and passed through a short column of "Florisil." The eluate was taken to dryness and the residue rechromatographed in 1 : 1 benzene–chloroform on "Florisil." The dark brown oil remaining after removal of the solvent was dissolved in benzene. Addition of light petroleum caused more dark material to separate. The solution was decanted and evaporated to dryness. The oil remaining did not crystallize and was demethylated with hydriodic acid, giving the *amino-acid* (1·43 g., 12·5%) as colourless needles, m. p. 255—260° (decomp.), $[\alpha]_D^{20}$ −18° (Found: C, 36·4; H, 3·3; N, 2·4. $C_{17}H_{17}I_2NO_4$ requires C, 37·0; H, 3·1; N, 2·5%).

Ethyl 4-*Chloro*-3,5-*dinitrophenylacetate*.—Diethylaniline (45 ml.) was added dropwise to a solution of ethyl 4-hydroxy-3,5-dinitrophenylacetate [15] (25 g.) in phosphoryl chloride (54 ml.), and the solution heated on the steam-bath for 1¼ hr., then cooled. Unchanged phosphoryl chloride was destroyed with ethanol. The mixture was evaporated under reduced pressure and the residue extracted with chloroform. The chloroform was washed with 2N-hydrochloric acid, then with water, dried (Na_2SO_4), and evaporated, leaving a dark gum which was passed in benzene through alumina. Evaporation left an oil which was crystallized from ethanol, giving *ethyl* 4-*chloro*-3,5-*dinitrophenylacetate* (12·0 g., 41%), m. p. 71—73° (Found: C, 41·6; H, 2·9; Cl, 12·3; N, 9·6. $C_{10}H_9ClN_2O_6$ requires C, 41·8; H, 3·1; Cl, 12·0; N, 9·7%).

Ethyl 3,5-*Dinitro*-4-*phenylthiophenylacetate*.—(a) *From ethyl* 4-*chloro*-3,5-*dinitrophenylacetate*. The chloro-compound (1·0 g.) was refluxed for 30 min. with benzenethiol (0·36 ml.) and potassium hydroxide (214 mg.) in 95% ethanol (15 ml.). The mixture was cooled, diluted with water, and extracted with benzene. The benzene extract was washed with 2N-sodium hydroxide (30 ml.), then with water, dried, and evaporated. The residual oil was chromatographed on alumina. Elution with benzene gave first a dark red oil, then a pale yellow oil. The latter crystallized from 95% ethanol to give 300 mg. (24%) of a product, m. p. 51—53·5°, identical (infrared) with that described in (b).

(b) *From ethyl* 3,5-*dinitro*-4-*toluene*-p-*sulphonyloxyphenylacetate*. This sulphonate [15] (9·8 g.) in dry benzene (40 ml.) was refluxed for 30 min. with dry pyridine (6 ml.), the mixture cooled, and the benzene decanted. The residual gum, dissolved in chloroform (50 ml.) and pyridine (6 ml.), was refluxed for 16 hr. with benzenethiol (8·1 ml.). The mixture was diluted with chloroform and the solution washed with 2N-hydrochloric acid, 2N-sodium hydroxide, and water, dried (Na_2SO_4), and evaporated. The residual gum was dissolved in light petroleum (b. p. 60—80°) containing a trace of benzene and chromatographed on alumina (23 × 3 cm.). Elution with light petroleum containing 15% of benzene gave diphenyl disulphide, m. p. 57—59°. Further elution with benzene gave an orange oil (5·3 g.), which crystallized from alcohol giving *ethyl* 3,5-*dinitro*-4-*phenylthiophenylacetate* (5·0 g., 60%), m. p. 53—55° (Found: C, 52·7; H, 3·5; N, 8·4; S, 9·4. $C_{16}H_{14}N_2O_6S$ requires C, 53·0; H, 3·9; N, 7·9; S, 8·8%).

Ethyl 3,5-*Diamino*-4-*phenylthiophenylacetate*.—The preceding ester (3·0 g.) in acetic acid (25 ml.) was shaken in hydrogen in the presence of 5% palladium–charcoal (400 mg.). No hydrogen was taken up, so more catalyst (400 mg.) was added and shaking resumed. Hydrogenation was then complete in 12 hr. The catalyst was filtered off in nitrogen and the filtrate evaporated to dryness under reduced pressure. The residual gum crystallized from alcohol, giving the diamine, m. p. 87—89°, which rapidly darkened. The *diacetyl derivative* had m. p. 176—177° (Found: C, 62·9; H, 5·7; N, 7·1; S, 8·4. $C_{20}H_{22}N_2O_4S$ requires C, 62·3; H, 5·7; N, 7·3; S, 8·3%).

Ethyl 3,5-*Di-iodo*-4-*phenylthiophenylacetate*.—The diamine prepared from ethyl 3,5-dinitro-4-phenylthiophenylacetate (10 g.) was tetrazotized and the tetrazonium solution treated with iodine in potassium iodide solution.[4] The combined chloroform extracts were washed with sodium hydrogen sulphite solution, then with water, dried (Na_2SO_4), and evaporated. The

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residual gum was twice chromatographed in benzene on alumina and eluted with benzene. Removal of the benzene gave a pale yellow gum (9·05 g.) which crystallized from alcohol, giving *ethyl* 3,5-*di-iodo*-4-*phenylthiophenylacetate* (7·4 g., 50% from the dinitro-compound), m. p. 111—113° (Found: C, 37·0; H, 2·5; S, 6·3. $C_{16}H_{14}I_2O_2S$ requires C, 36·7; H, 2·7; S, 6·1%).

3,5-*Di-iodo*-4-*phenylthiophenylacetic Acid*.—6N-Hydrochloric acid (75 ml.) was added to a hot solution of the preceding ester (5·5 g.) in glacial acetic acid (120 ml.). The mixture was refluxed for 1½ hr. On cooling, the solution deposited 3,5-*di-iodo*-4-*phenylthiophenylacetic acid* (4·6 g., 88%), m. p. 187—189° (Found: C, 33·9; H, 2·0; I, 51·3; S, 6·5. $C_{14}H_{10}I_2O_2S$ requires C, 33·8; H, 2·0; I, 51·2; S, 6·4%).

Ethyl Ester of N-*Acetyl*-4-p-*methoxyphenylthio*-3,5-*dinitro*-D-*phenylalanine*.—*N*-Acetyl-3,5-dinitro-D-tyrosine ethyl ester (10·0 g.) was converted into the toluene-*p*-sulphonate.[4] This was refluxed in benzene (44 ml.) for 30 min. with pyridine (6·8 ml.), then cooled to 0° and the benzene was decanted. The residual gum, dissolved in chloroform (50 ml.) and pyridine (7·4 ml.), was refluxed for 16 hr. with *p*-methoxybenzenethiol (8·2 g., 2 equiv.). The mixture was diluted with chloroform (150 ml.) and washed with 2N-hydrochloric acid, 2N-sodium hydroxide, and water, dried ($MgSO_4$), and evaporated. The residual solid recrystallized from benzene–light petroleum (b. p. 60—80°), giving the pale yellow *ester* (10·0 g., 74%), m. p. 146—150° (Found: C, 51·8; H, 4·7; N, 9·4; S, 7·1. $C_{20}H_{21}N_3O_8S$ requires C, 51·8; H, 4·5; N, 9·1; S, 6·9%).

Ethyl Ester of N-*Acetyl*-3,5-*diamino*-4-p-*methoxyphenylthio*-D-*phenylalanine*.—Hydrogenation of the preceding ester (15·0 g.) gave the diamine as a pale brown solid (10·8 g., 83%). The *diacetyl derivative* had m. p. 217·5—220·5 (Found: C, 59·0; H, 5·9; N, 9·1; S, 6·1. $C_{24}H_{29}N_3O_6S$ requires C, 59·2; H, 5·9; N, 8·6; S, 6·6%).

Ethyl Ester of N-*Acetyl*-3,5-*di-iodo*-4-p-*methoxyphenylthio*-D-*phenylalanine*.—The preceding diamine (10·0 g.) was tetrazotized and treated with iodine in potassium iodide,[4] giving the *di-iodo-ester* (6·3 g., 41%), m. p. 148—150° (from ethanol) (Found: C, 38·3; H, 3·6; I, 40·0. $C_{20}H_{21}I_2NO_4S$ requires C, 38·4; H, 3·4; I, 40·6%).

4-p-*Hydroxyphenylthio*-3,5-*di-iodo*-D-*phenylalanine*.—The preceding ester (15·4 g.), refluxed for 2 hr. with 6N-hydrobromic acid (300 ml.) in glacial acetic acid (300 ml.), gave 4-p-*hydroxyphenylthio*-3,5-*di-iodo*-D-*phenylalanine* (6·32 g., 51%), m. p. 239—244° (decomp.), $[\alpha]_D^{20}$ −24·5° (*c* 2) (Found: C, 32·8; H, 2·6; I, 45·0. $C_{15}H_{13}I_2NO_3S$ requires C, 33·3; H, 2·4; I, 46·9%).

4-(4-*Hydroxy*-3,5-*di-iodophenylthio*)-3,5-*di-iodo*-D-*phenylalanine*.—The di-iodo-compound (2·0 g.) was dissolved in aqueous 33% ethylamine (50 ml.), and a N-solution of iodine in potassium iodide (22 ml., 50% excess) was added to the stirred solution during 45 min. at 25—30°. The solution was left overnight, then evaporated to dryness under reduced pressure. The residue was treated with charcoal and a little sodium hydrogen sulphite in dilute hydrochloric acid and ethanol and neutralized at the b. p. with sodium acetate. The crystalline *tetra-iodo-acid* was filtered off and washed with ethyl acetate until almost colourless [1·5 g., 51%; m. p. 230—233° (decomp.)] (Found: C, 23·2; H, 1·8; I, 60·2. $C_{15}H_{11}I_4NO_3S,\frac{1}{2}EtOH$ requires C, 23·5; H, 1·7; I, 62·3%).

4-(4-*Hydroxy*-3-*iodophenylthio*)-3,5-*di-iodo*-D-*phenylalanine*.—The di-iodo-compound (2·0 g.) was dissolved in aqueous 33% ethylamine (50 ml.), and a N-solution of iodine in potassium iodide (8·0 ml.) added to the stirred solution during 45 min. at 25—30°. The mixture was worked up as above, giving the tri-iodo-acid (0·5 g., 20%). This contained <3% of the di-iodo- and <2% of the tetraiodo-compound (Found: C, 28·1; H, 2·3; I, 52·1; N, 1·9. Calc. for $C_{15}H_{12}I_3NO_3S,EtOH$: C, 28·6; H, 2·5; I, 53·4; N, 1·9%).

4-*Chloromethyl*-2,6-*di-iodo*-4′-*methoxybiphenyl*.—4-Hydroxymethyl-2,6-di-iodo-4′-methoxybiphenyl [11] (2·34 g.) in chloroform (14 ml.) was cooled to 0°. Phosphorus pentachloride (1·25 g.) was added in small portions with stirring which was continued at room temperature for a further 90 min. The solution was washed with water, dilute sodium hydrogen carbonate solution, then water, dried ($MgSO_4$), and evaporated under reduced pressure. The resulting oil crystallized from alcohol, giving 4-chloromethyl-2,6-di-iodo-4′-methoxybiphenyl (1·75 g., 72%), m. p. 108—109°.

4-*Cyanomethyl*-2,6-*di-iodo*-4′-*methoxybiphenyl*.—The preceding compound (10·32 g.), in ethanol (100 ml.) containing a trace of potassium iodide, was mixed with potassium cyanide (2·5 g.) in water (5 ml.) and refluxed for 4½ hr. The solution was concentrated under reduced pressure and diluted with water, giving 4-cyanomethyl-2,6-di-iodo-4′-methoxybiphenyl (10·0 g., 99%), with no definite m. p. (Found: C, 39·1; H, 2·6. Calc. for $C_{15}H_{11}I_2NO$: C, 38·0; H, 2·3%). This material could not be recrystallized.

3,5-*Di-iodophenyl*-4-p-*hydroxyphenylacetic Acid*.—The preceding compound (10·0 g.) was

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refluxed for 1½ hr. with glacial acetic acid (18 ml.) and constant-boiling hydriodic acid (90 ml.). Some of the solvent was removed under reduced pressure and aqueous sodium hydrogen sulphite solution added. The brown product which separated was dissolved in the minimum volume of hot acetone and reprecipitated with dilute aqueous sodium hydrogen sulphite, giving 10·12 g. of pale yellow material. This was dissolved in alcohol (charcoal), filtered, and taken to dryness, then crystallized from benzene containing a little acetone, giving an *acid* (7·2 g., 72%), m. p. 238—242° (Found: C, 35·1; H, 2·2; I, 52·9. $C_{14}H_{10}I_2O_3$ requires C, 35·0; H, 2·1; I, 52·9%).

3,5-*Di-iodophenyl*-4-(4-*hydroxy*-3,5-*di-iodophenyl*)*acetic Acid*.—The preceding compound (0·5 g.) was dissolved in 33% (w/v) aqueous ethylamine (10 ml.) and a 0·99N-solution of iodine in potassium iodide (6·3 ml.) was added to the stirred solution during 20 min. at 28—30°. After 1 hr. the solution was made just acid with hydrochloric acid, and the precipitate filtered off, washed with water, dried (0·77 g.), and recrystallized from acetic acid, giving the *tetraiodo-acid* (0·61 g., 80%), m. p. 232—233° (decomp.) (Found: C, 23·3; H, 1·2; I, 69·8. $C_{14}H_8I_4O_3$ requires C, 23·0; H, 1·1; I, 69·4%).

3,5-*Di-iodophenyl*-4-(4-*hydroxy*-3-*iodophenyl*)*acetic Acid*.—The di-iodo-acid (6·0 g.) was dissolved in 33% (w/v) aqueous ethylamine (50 ml.) and a 0·99N-solution of iodine in potassium iodide (29·0 ml.) added during 35 min. at 29°. The solution was worked up as in the last experiment, giving the tri-iodo-acid (2·28 g., 30%), m. p. 210—211° (decomp.) (Found: C, 28·4; H, 1·95; I, 62·0. Calc. for $C_{14}H_9I_3O_3$: C, 27·75; H, 1·5; I, 62·8%). This material contained less than 5% each of di-iodo- and tetraiodo-acid.

4-*Acetoxymethyl*-2,6-*dichloro*-4′-*methoxybiphenyl*.—2,6-Diamino-4-hydroxymethyl-4′-methoxybiphenyl (5·0 g.) was tetrazotized, and the tetrazonium salt decomposed with cuprous chloride, giving a dark red oil. This was heated on the steam-bath for 1 hr. with acetic anhydride. Excess of acetic anhydride was removed under reduced pressure and the residue (5·64 g.) in benzene was chromatographed on " Florisil " (100 g.). Evaporation of the eluate and treatment of the product with charcoal in ethanol gave 5·13 g. of crude solid. 1·5 g. of this material were crystallized from aqueous ethanol, then from isopropyl ether, giving 4-*acetoxymethyl*-2,6-*dichloro*-4′-*methoxybiphenyl* (0·44 g., 22%), m. p. 57—59° (Found: C, 59·3; H, 4·6; Cl, 21·65. $C_{16}H_{14}Cl_2O_3$ requires C, 59·1; H, 4·3; Cl, 21·8%). The product also crystallized from isopropyl ether in 35% yield, giving material of m. p. 52—55°.

2,6-*Dichloro*-4-*hydroxymethyl*-4′-*methoxybiphenyl*.—Alkaline hydrolysis of the preceding compound, m. p. 52—55° (9·3 g.), gave 8·1 g. (100%) of a straw-coloured oil.

2,6-*Dichloro*-4-*chloromethyl*-4′-*methoxybiphenyl*.—Crude 2,6-dichloro-4-hydroxymethyl-4′-methoxybiphenyl (8·0 g.) in chloroform (180 ml.) was stirred, and phosphorus pentachloride (8·0 g.) added at 0—5°. The solution was left at room temperature for 1½ hr., then washed with water and dilute sodium hydrogen carbonate solution, dried, and evaporated under reduced pressure. The resulting oil crystallized from ethanol, giving 2,6-*dichloro*-4-*chloromethyl*-4′-*methoxybiphenyl* (5·92 g., 70%), m. p. 82—83°. A sample recrystallized from ethanol had m. p. 86—87° (Found: C, 56·1; H, 3·7; Cl, 35·1. $C_{14}H_{11}Cl_3O$ requires C, 55·75; H, 3·7; Cl, 35·3%).

2,6-*Dichloro*-4-*cyanomethyl*-4′-*methoxybiphenyl*.—The preceding compound (m. p. 82—83°) (1·0 g.) was dissolved in ethanol (10 ml.) containing a trace of potassium iodide and refluxed for 4½ hr. with potassium cyanide (0·36 g.) in water (0·7 ml.). Some of the solvent was removed under reduced pressure, then the solution was diluted with water and extracted with ether. The extract was washed with water, dried, and evaporated under reduced pressure, leaving a straw-coloured oil (0·97 g.).

2,6-*Dichloro*-4′-*hydroxy*-4-*biphenylylacetic Acid*.—The preceding compound (5·48 g.), demethylated with hydriodic acid, underwent simultaneous hydrolysis and gave the named *biphenylylacetic acid* (2·89 g., 52%), m. p. 182—186° (Found: C, 56·65; H, 3·4; Cl, 23·9. $C_{14}H_{10}Cl_2O_3$ requires C, 56·6; H, 3·4; Cl, 23·9%).

3,5-*Dichloro*-4-(3-*chloro*-4-*hydroxyphenoxy*)*benzoic Acid*.—3,5-Dichloro-4-*p*-hydroxyphenoxybenzoic acid (5·00 g.) was treated in glacial acetic acid (750 ml.) with a freshly prepared solution of chlorine (1·19 g.) in glacial acetic acid (26 ml.) in one portion with vigorous stirring. After 20 min. (negative starch–iodide reaction) the acid was removed under reduced pressure and the residue dissolved in acetic acid and filtered. Water was added to the hot solution until precipitation started, the solution was cooled, and a little solid was filtered off. The hot filtrate was again diluted with water and cooled. The colourless trichloro-acid separated (4·7 g., 80%), having m. p. 180—184° (Found: C, 46·7; H, 2·3; Cl, 30·9. Calc. for $C_{13}H_7Cl_3O_4$: C, 46·7; H, 2·1; Cl, 31·9%). This material contained <5% each of the dichloro- and tetrachloro-acid.

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4-(4-*Hydroxy*-3-*iodophenoxy*)-3,5-*di-iodobenzoic Acid*.—4-*p*-Hydroxyphenoxy-3,5-di-iodobenzoic acid [16] (10·0 g.) was dissolved in aqueous 33% ethylamine (100 ml.) and a N-solution of iodine in potassium iodide (42 ml.) added, with stirring, during 1½ hr. at 25—30°. Ice (200 g.) was then added and the mixture shaken with ethyl acetate. Concentrated hydrochloric acid (60 ml.) was added and the mixture shaken again. The organic layer was separated and the aqueous layer extracted three times with ethyl acetate. The combined extracts (total vol. 300 ml.) were washed with sodium chloride solution, dried ($MgSO_4$), and evaporated under reduced pressure. The residual oil was dissolved in ethanol (30 ml.), and a solution of diethanolamine (2·65 g.) in ethanol (10 ml.) added. The mixture was refrigerated overnight and the precipitated diethanolamine salt recrystallized from ethanol.

This salt was decomposed in water with hydrochloric acid and the organic acid extracted into ethyl acetate. The extract was washed with sodium chloride solution, dried ($MgSO_4$), and evaporated under reduced pressure. The *tri-iodo-acid* separated and was recrystallized from aqueous ethanol, giving 4·4 g. (35%) of material, m. p. 259—261·5° (Found: C, 25·5; H, 1·2; I, 62·7. $C_{13}H_6I_3O_4$ requires C, 25·7; H, 1·0; I, 62·8%).

3,5-*Dibromo*-4-p-*methoxyphenoxyphenylacetic Acid*.—3,5-Dinitro-4-*p*-methoxyphenoxyphenylacetic acid (9·8 g.) was reduced and the diamine tetrazotized as described by Meltzer *et al.*[15] The tetrazonium solution was added in a thin stream to a stirred solution of cuprous bromide (20 g.) in aqueous 50% w/v hydrobromic acid (300 ml.) containing chloroform (200 ml.). Stirring was continued for 45 min., water (300 ml.) added, the chloroform separated, and the aqueous layer again extracted with chloroform. The combined chloroform extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness. The residue (11 g.) was dissolved in cold benzene, and light petroleum was added; the solution was poured off from a dark oil, and this process repeated until a pale yellow solution was obtained. The solution was evaporated to dryness and the residue crystallized from aqueous acetic acid. The *dibromo-acid* (7·8 g., 78%) separated as off-white crystals, m. p. 142—143·5° (Found: Br, 37·6. $C_{15}H_{12}Br_2O_4$ requires Br, 38·4%).

3,5-*Dibromo*-4-(p-*hydroxyphenoxy*)*phenylacetic Acid*.—The preceding compound (9·1 g.) was refluxed in acetic acid saturated with hydrogen bromide (250 ml.) for 1¾ hr. The solvent was removed under reduced pressure and the residue boiled in ethanol (150 ml.) with charcoal. The filtered solution was evaporated, leaving an almost colourless solid, which recrystallized from benzene containing a little acetone. The *dibromo-acid* (6·2 g.) had m. p. 215—217° (Found: Br, 39·0. $C_{14}H_{10}Br_2O_4$ requires Br, 39·7%).

3,5-*Dichloro*-4-(3-*chloro*-4-*hydroxyphenoxy*)*phenylacetic Acid*.—3,5-Dichloro-4-*p*-hydroxyphenoxyphenylacetic acid (0·962 g.) in acetic acid (50 ml.) was treated dropwise with a 0·0905M-solution of chlorine in carbon tetrachloride (7·00 ml., 1·03 equiv.) with stirring at room temperature. After 2 hr. the solvent was removed under reduced pressure and the residual oil crystallized from benzene–light petroleum, giving the trichloro-acid (1·00 g., 93%), m. p. 146—148° (Found: C, 48·5; H, 2·7; Cl, 30·5. Calc. for $C_{14}H_9Cl_3O_4$: C, 48·4; H, 2·6; Cl, 30·6%). This material contained not more than 6% and 3% respectively of the di- and tetra-chloro-compounds.

3,5-*Dichloro*-4-(3,5-*dichloro*-4-*hydroxyphenoxy*)*phenylacetic Acid*.—Treatment of the dichloro-acid with 2·5 equiv. of chlorine as in the preceding preparation gave a solid, which was recrystallized twice from benzene–light petroleum. The *tetrachloro-acid* separated as prisms, m. p. 180—185° (23% yield) (Found: C, 44·3; H, 2·3; Cl, 37·4. $C_{14}H_8Cl_4O_4$ requires C, 44·0; H, 2·1; Cl, 37·2%).

3,5-*Dibromo*-4-(3-*bromo*-4-*hydroxyphenoxy*)*phenylacetic Acid*.—Treatment of the dibromo-acid with 0·99 equiv. of bromine in acetic acid as in the preceding preparation gave the *tribromo-acid*, m. p. 166—168° (from benzene–light petroleum) (83%) (Found: C, 35·0; H, 2·0; Br, 50·1. $C_{14}H_9Br_3O_4$ requires C, 35·0; H, 1·9; Br, 50·0%). This material contained <1% and <2% respectively of the dibromo- and tetrabromo-acid.

3,5-*Dibromo*-4-(3,5-*dibromo*-4-*hydroxyphenoxy*)*phenylacetic Acid*.—The dibromo-acid (0·50 g.) in acetic acid (50 ml.) was treated with bromine in acetic acid (4·4 ml.; 10% w/v solution; 2·2 equiv.) at room temperature, with stirring, and left overnight. More bromine in acetic acid (2·0 ml.; 10% solution) was added, and the mixture left at 50—60° for 8 hr., then at room temperature overnight. The solvent was removed and the residue recrystallized from acetone and benzene, giving almost colourless needles (300 mg., 52%), m. p. 200—203°, of the *product* (Found: C, 29·95; H, 1·4; Br, 56·9. $C_{14}H_8Br_4O_4$ requires C, 30·0; H, 1·4; Br, 57·2%).

[15] Clayton, Green, and Hems, *J.*, 1951, 2467.

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Ethyl Ester of N-*Acetyl*-3,5-*dinitro*-4-*phenoxy*-D-*phenylalanine*.—This *compound*, prepared by methods similar to those used for the L-compound,[17] had m. p. 139·5—141°, $[\alpha]_D^{21}$ −45·3° (Found: N, 10·1. $C_{19}H_{19}N_3O_8$ requires N, 10·1%). For the L-compound, Barnes *et al.*[17] report m. p. 136—137°, $[\alpha]_D^{22}$ +44·9°.

3,5-*Di-iodo*-4-*phenoxy*-D-*phenylalanine*.—The preceding compound was reduced, and the diamine (not isolated) converted by known methods [17] into the *di-iodo-compound*, m. p. 249—250° (decomp.), $[\alpha]_D^{22}$ −29·7° (Found: C, 35·1; H, 2·6; N, 2·6; I, 49·3. $C_{15}H_{13}I_2NO_4$ requires C, 35·4; H, 2·6; N, 2·8; I, 49·9%). For the DL-compound, Barnes *et al.*[17] report m. p. 237—238°.

Ethyl Ester of N-*Acetyl*-3,5-*dibromo*-4-p-*methoxyphenoxy*-D- *and* -L-*phenylalanine*.—*N*-Acetyl-3,5-diamino-4-*p*-methoxyphenoxy-L-phenylalanine ethyl ester (19·3 g.) was tetrazotized as described by Chalmers *et al.*[4] The tetrazonium solution was added in a slow stream to a stirred solution of cuprous bromide (24 g.) in aqueous 50% w/v hydrobromic acid (320 ml.) containing chloroform (200 ml.). The mixture was worked up as above, and the residual brown gum (26·1 g.) recrystallized from isopropyl alcohol (18 ml.), giving the *dibromo-ester* (21·1 g., 82%), m. p. 113—115° (Found: Br, 30·65; N, 3·05. $C_{20}H_{21}Br_2NO_5$ requires Br, 31·0; N, 2·7%). The D-*compound*, prepared similarly, had m. p. 112·5—115° (Found: Br, 30·9%).

3,5-*Dibromo*-D- *and* -L-*thyronine*.—The preceding D-compound (1·0 g.) was demethylated with hydriodic acid, giving colourless 3,5-*dibromo*-D-*thyronine* (0·63 g., 75%), m. p. 262—265° (decomp.), $[\alpha]_D^{23}$ −30·5° (Found: N, 3·2. $C_{15}H_{13}Br_2NO_4$ requires N, 3·25%). The L-*amino-acid*, prepared similarly, had m. p. 262—265° (decomp.), $[\alpha]_D^{20}$ +29·9° (Found: C, 41·7; H, 3·2. $C_{15}H_{13}Br_2NO_4$ requires C, 41·7; H, 3·0%).

3,5,3′-*Tribromo*-D- *and* -L-*thyronine*.—3,5-Dibromo-D-thyronine (8·0 g.) in glacial acetic acid (370 ml.) and 2N-hydrochloric acid (185 ml.) was stirred and treated at room temperature with bromine (2·85 g.) in acetic acid (28 ml.). After 30 min. the acids were removed and the residue crystallized twice from 2N-hydrochloric acid. The hydrochloride in hot 70% ethanol was neutralized with sodium acetate solution. 3,5,3′-*Tribromo*-D-*thyronine* separated (4·27 g., 45%), having m. p. 239—245°, $[\alpha]_D^{20}$ −28° (Found: C, 35·1; H, 2·6; Br, 47·0. $C_{15}H_{12}Br_3NO_4$ requires C, 35·3; H, 2·3; Br, 47·0%). 3,5,3′-*Tribromo*-L-*thyronine*, prepared similarly, had m. p. 233—234°, $[\alpha]_D^{20}$ +28° (Found: Br, 47·1%).

3,5,3′,5′-*Tetrabromo*-D- *and* -L-*thyronine*.—3,5,-Dibromo-D-thyronine (5·7 g.) in acetic acid (120 ml.) was treated with bromine (4·2 g.) in acetic acid (40 ml.). Removal of solvent left a residue shown by chromatography to contain some tribromothyronine. The residue was dissolved in glacial acetic acid (100 ml.), and bromine (1·6 g.) in acetic acid (16 ml.) added, at 100°, to the stirred solution. The solution was allowed to cool overnight, the solvent removed, and the residue dissolved in 70% ethanol. Addition of sodium acetate solution at the b. p. gave 3,5,3′,5′-*tetrabromo*-D-*thyronine* (3·4 g., 35%), m. p. 207—211°, $[\alpha]_D^{20}$ −11·5° (*c* 1 in dioxan containing 10% of 2N-hydrochloric acid) (Found: N, 2·2; Br, 54·5. $C_{15}H_{11}Br_4NO_4$ requires N, 2·4; Br, 54·4%). 3,5,3′,5′-*Tetrabromo*-L-*thyronine*, prepared similarly, was obtained as the hydrate, m. p. 233—236°, $[\alpha]_D^{20}$ +10° (Found: Br, 52·3. $C_{15}H_{11}Br_4NO_4,H_2O$ requires Br, 52·7%).

3,5,3′-*Trichloro*-D- *and* -L-*thyronine*.—3,5-Dichloro-D-thyronine (11·2 g.) was dissolved in glacial acetic acid (1 l.) by passing in a little hydrogen chloride, and a freshly prepared solution of chlorine (2·33 g.) in acetic acid (70 ml.) was added, with shaking, during 2 min. After 30 min. at room temperature (negative starch–iodide reaction) the acids were removed and the residue boiled in 2N-hydrochloric acid (390 ml.) with charcoal and filtered. The filtrate, on cooling, deposited the hydrochloride. This was dissolved in 2N-hydrochloric acid (196 ml.), and the solution brought at the b. p. to pH 5 with sodium acetate. 3,5,3′-*Trichloro*-D-*thyronine* (10·0 g., 81%) separated as colourless needles, m. p. 238—241°, $[\alpha]_D^{20}$ −36° (Found: C, 47·5; H, 3·6; Cl, 27·7; N, 3·8. $C_{15}H_{12}Cl_3NO_4$ requires C, 47·8; H, 3·2; Cl, 28·4; N, 3·7%). This material contained <2% each of dichloro- and tetrachloro-thyronine. 3,5,3′-*Trichloro*-L-*thyronine*, prepared similarly, had m. p. 244—247°, $[\alpha]_D^{20}$ +33° (Found: Cl, 28·4%).

3,5,3′,5′-*Tetrachloro*-D-*thyronine*.—3,5-Dichloro-D-thyronine (1·3 g.) was dissolved in glacial acetic acid (50 ml.) by passing in a little hydrogen chloride, and a freshly prepared solution of chlorine (0·27 g.) in acetic acid (16 ml.) added, with shaking, during 2 min. The solution was left for 1½ hr., then cooled to 8°. Chlorine was passed in slowly, with stirring, for ½ hr., the hydrochloride separating. The solution was then set aside for ½ hr., next air was bubbled through it, and the cooling-bath removed. When no more chlorine was present the precipitate was collected and dissolved in 0·5N-hydrochloric acid; sodium acetate was added to the boiling

[17] Barnes, Elks, Stephens, and Waller, *J.*, 1953, 764.

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solution until the pH was 5. 3,5,3′,5′-*Tetrachloro*-D-*thyronine* (0·89 g., 57%) separated as colourless crystals, m. p. 240° (decomp.), $[\alpha]_D^{20}$ −32·2° (Found: C, 43·6; H, 3·1; Cl, 34·1; N, 3·4. $C_{15}H_{11}Cl_4NO_4$ requires C, 43·8; H, 2·7; Cl, 34·5; N, 3·4%). 3,5,3′,5′-*Tetrachloro*-L-*thyronine*, obtained similarly, had m. p. 233—234·5°, $[\alpha]_D^{20}$ +31° (Found: Cl, 34·3%).

3,5,3′-*Trichloro*-5′-*iodo*-D-*thyronine*.—3,5,3′-Trichloro-D-thyronine (4·0 g.) in aqueous 33% w/v ethylamine (100 ml.) was stirred and treated at 25—30° with a 1·05N-solution of iodine in potassium iodide (30 ml.) during 1 hr. After 1 hr. more the pH was adjusted to 5 with 10N-hydrochloric acid. The hydrochloride recrystallized from a little 2N-hydrochloric acid (charcoal), and the product was dissolved in 0·5N-hydrochloric acid and neutralized at the b. p. with aqueous sodium acetate. 3,5,3′-Trichloro-5′-iodo-D-thyronine separated (2·1 g., 39%), having m. p. 206—208° (Found: C, 36·4; H, 2·7; I, 24·4. Calc. for $C_{15}H_{11}Cl_3INO_4$: C, 35·8; H, 2·2; I, 25·3%).

3′-*Bromo*-3,5-*dichloro*-D-*thyronine*.—3,5-Dichloro-D-thyronine (1·0 g.), dissolved in acetic acid (50 ml.) containing a little dry hydrogen chloride, was treated at room temperature with bromine (0·47 g.) in acetic acid (7·4 ml.). After 16 hr. the solvent was removed, the residue dissolved in boiling aqueous ethanol, and sodium acetate solution added. The *bromo-compound* separated (1·14 g., 92%), having m. p. 242—244°, $[\alpha]_D^{20}$ −32·2° (Found: C, 42·95; H, 3·1. Hal, 34·7; N, 3·6. $C_{15}H_{12}BrCl_2NO_4$ requires C, 42·8; H, 2·9; Hal, 35·8; N, 3·3%). This material contained <1% of dichloro- and <2% of dibromodichloro-thyronine.

3′,5′-*Dibromo*-3,5-*dichloro*-D-*thyronine*.—3,5-Dichloro-D-thyronine (1 g.), treated as in the last preparation with bromine (1·4 g.) at room temperature for 70 hr., gave 3′,5′-*dibromo*-3,5-*dichloro*-D-*thyronine* (1·28 g., 87%), m. p. 235° (decomp.), $[\alpha]_D^{20}$ −27·5° (Found: C, 35·8; H, 2·4; Hal, 46·5; N, 2·5. $C_{15}H_{11}Br_2Cl_2NO_4$ requires C, 36·0; H, 2·2; Hal, 46·15; N, 2·8%).

3,5-*Dichloro*-3′-*iodo*-D-*thyronine*.—Treatment of 3,5-dichloro-D-thyronine (5·0 g.) in aqueous 33% ethylamine (40 ml.) with a 1·05N-solution of iodine in potassium iodide (30 ml.) during 1 hr. at 25—30°, then neutralization to pH 5 with hydrochloric acid, recrystallization from 2N-hydrochloric acid, and neutralization with sodium acetate, gave 3,5-*dichloro*-3′-*iodo*-D-*thyronine* (2·8 g., 41%), m. p. 197—200°, $[\alpha]_D^{20}$ −27° (Found: C, 38·9; H, 4·0; I, 27·8. $C_{15}H_{12}Cl_2INO_4$ requires C, 38·4; H, 3·8; I, 27·1%). This material contained 1% of dichlorothyronine and 2% of dichlorodi-iodothyronine.

3,5-*Dichloro*-3′,5′-*di-iodo*-D-*thyronine*.—Treatment of 3,5-dichloro-D-thyronine (5·0 g.) with a 1·05N-solution of iodine in potassium iodide (75·8 ml.) as above gave 3,5-*dichloro*-3′,5′-*di-iodo*-D-*thyronine* (3·03 g., 38%), m. p. 205—210° (decomp.) (Found: C, 30·2; H, 2·1; I, 42·5. $C_{15}H_{11}Cl_2I_2NO_4$ requires C, 30·3; H, 1·8; I, 42·7%).

3-*Chloro*-5,3′,5′-*tri-iodo*-D- *and* -L-*thyronine*.—3-Chloro-5-iodo-D-thyronine [18] (2·0 g.) in 33% aqueous ethylamine (40 ml.) was treated with a N-solution of iodine in potassium iodide (28·0 ml.) at room temperature. After 3 hr. the pH was adjusted to 5 with hydrochloric acid and the solid dissolved in hot ethanol containing a little 2N-sodium hydroxide. Neutralization with N-hydrochloric acid gave 3-chloro-5,3′,5′-tri-iodo-D-thyronine (2·62 g., 83%), m. p. 211—213° (decomp.), $[\alpha]_D^{20}$ −13·2° (Found: C, 27·0; H, 1·9; I, 52·5. Calc. for $C_{15}H_{11}ClI_3NO_4,\frac{1}{4}EtOH$: C, 27·1; H, 2·0; I, 53·7; N, 2·0%). 3-*Chloro*-5,3′,5′-*tri-iodo*-L-*thyronine*, prepared similarly, had m. p. 212—213° (Found: C, 27·4; H, 2·0; N, 1·9%).

3,5-*Dibromo*-3′-*chloro*-D-*thyronine*.—3,5-Dibromo-D-thyronine hydrochloride (4·0 g.) in glacial acetic acid (220 ml.) was treated at room temperature with chlorine (0·61 g.) in acetic acid (22 ml.). After 2 hr. the acetic acid was removed and the residue crystallized from 2N-hydrochloric acid, then redissolved in hydrochloric acid and neutralized at the b. p. with sodium acetate solution. 3,5-*Dibromo*-3′-*chloro*-D-*thyronine* separated as colourless crystals (2·8 g., 65%), m. p. 238—241° (Found: C, 38·8; H, 2·6; Hal, 41·9. $C_{15}H_{12}Br_2ClNO_4$ requires C, 38·4; H, 2·6; Hal, 41·9%). This material contained <2% each of dibromo- and dibromodichloro-thyronine.

3,5,3′-*Tribromo*-5′-*iodo*-D-*thyronine*.—3,5,3′-Tribromo-D-thyronine (4·0 g.) in aqueous 33% ethylamine (75 ml.) was treated at room temperature with a N-solution of iodine in potassium iodide (20 ml.) during 45 min. Most of the ethylamine solution was distilled off under reduced pressure and the remaining solution neutralized at 0° with 10N-hydrochloric acid. The hydrochloride separated and recrystallized (charcoal) from 2N-hydrochloric acid containing a little ethanol; it was then dissolved in 0·2N-hydrochloric acid and ethanol and neutralized with sodium acetate solution. 3,5,3′-*Tribromo*-5′-*iodo*-D-*thyronine* separated as colourless crystals

[18] Dibbo, Stephenson, Walker, and Warburton, *J.*, 1961, 2645.

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(2·2 g., 44%), m. p. 198—201° (Found: C, 28·8; H, 1·7; I, 19·5. $C_{15}H_{11}Br_2INO_4$ requires C, 28·3; H, 1·7; I, 20·0%).

*3,5-Dibromo-3′-iodo-*D*-thyronine.*—3,5-Dibromo-D-thyronine hydrochloride (1·27 g.) in aqueous 33% ethylamine (50 ml.) was treated with a N-solution of iodine in potassium iodide (5·4 ml.). After 3 hr. the pH was adjusted to 5 with 10N-hydrochloric acid below 25° and the precipitated hydrochloride redissolved in hot 0·5N-hydrochloric acid containing a little ethanol, then neutralized with sodium acetate. The impure amino-acid (1·34 g., 88%) was crystallized from N-hydrochloric acid containing a little ethanol, and the resulting hydrochloride neutralized with sodium acetate as before, giving 3,5-dibromo-3′-iodo-D-thyronine (0·97 g., 63%), m. p. 223—225° (decomp.), $[\alpha]_D^{22}$ −22·5° (Found: C, 32·0; H, 2·3; Hal, 52·0; I, 23·4; N, 2·2. Calc. for $C_{15}H_{12}Br_2INO_4$: C, 32·35; H, 2·15; Hal, 51·5; I, 22·8; N, 2·5%). This material contained 1% of dibromo- and 6% of dibromodi-iodo-thyronine.

*3,5-Dibromo-3′,5′-di-iodo-*D*-thyronine.*—3,5-Dibromo-D-thyronine hydrochloride (1·50 g.) in aqueous 33% ethylamine (100 ml.) was treated with a 1·06N-solution of iodine in potassium iodide (19 ml.) at room temperature. Next day the pH was adjusted to 5 at 10° by adding 5N-hydrochloric acid. The pale yellow precipitate was dried and washed with hot ethanol (3 × 20 ml.), leaving 3,5-dibromo-3′,5′-di-iodo-D-thyronine as a cream powder (1·70 g., 77%), m. p. 195—198° (decomp.), $[\alpha]_D^{20}$ −22·5° (Found: C, 26·8; H, 2·1; Hal, 58·6; I, 35·8. Calc. for $C_{15}H_{11}Br_2I_2NO_4$: C, 26·4; H, 1·6; Hal, 60·6; I, 37·2%).

*3′-Chloro-3,5-di-iodo-*D*-thyronine.*—3,5-Di-iodo-D-thyronine (5·25 g.) was dissolved in glacial acetic acid (500 ml.) by passing in a little hydrogen chloride. Chlorine (0·71 g.) in acetic acid (70 ml.) was added in one portion, at room temperature, with shaking. After 30 min. (negative starch–iodide reaction) the acetic acid was removed under reduced pressure and the residue recrystallized twice from 2N-hydrochloric acid (80 ml.) and ethanol (15 ml.) (charcoal). The resulting hydrochloride (4·4 g.) was dissolved in hydrochloric acid and ethanol and neutralized with sodium acetate solution. *3′-Chloro-3,5-di-iodo-*D*-thyronine* separated as colourless needles (3·53 g., 63%), m. p. 256° (decomp.), $[\alpha]_D^{20}$ −23·0° (Found: C, 32·0; H, 2·2; Cl, 6·3; I, 45·4. $C_{15}H_{12}Cl_2INO_4$ requires C, 32·2; H, 2·2; Cl, 6·3; I, 45·4%). This compound contained <2% each of di-iodo- and dichlorodi-iodo-thyronine.

*3′,5′-Dichloro-3,5-di-iodo-*D*-thyronine.*—3,5-Di-iodo-D-thyronine (5·25 g.) in glacial acetic acid (500 ml.) containing a little hydrogen chloride was treated with chlorine (0·8 g.) in acetic acid (70 ml.). After 30 min. the mixture was cooled to 10° and chlorine passed slowly through the supercooled solution for 1 hr. The excess of chlorine was removed by bubbling air through the solution, then the solvent was removed under reduced pressure. The residue was boiled with 0·5N-hydrochloric acid (500 ml.), ethanol (75 ml.), and sodium hydrogen sulphite, and the solution decanted from some tar and again treated with charcoal and sodium hydrogen sulphite. The cooled solution deposited the hydrochloride as a grey solid (2·8 g.) which recrystallized from 0·5N-hydrochloric acid (charcoal); it was neutralized with sodium acetate. 3′,5′-Dichloro-3,5-di-iodo-D-thyronine was obtained in 30% overall yield as colourless needles, m. p. 261—262° (decomp.), $[\alpha]_D^{20}$ −23·6° (Found: C, 29·7; H, 2·3; Hal, 55·8; N, 2·1. Calc. for $C_{15}H_{11}Cl_2I_2NO_4,H_2O$: C, 29·4; H, 2·1; Hal, 54·8; N, 2·3%).

*3′-Bromo-3,5-di-iodo-*D*-thyronine.*—3,5-Di-iodo-D-thyronine (3·0 g.) in glacial acetic acid (150 ml.) containing a little hydrogen chloride was treated at room temperature with bromine (0·91 g.) in acetic acid (9·5 ml.) and left for 20 hr. The solvent was removed under reduced pressure and the residue dissolved in hot aqueous ethanol (2 l.) containing a little hydrochloric acid. Neutralization with sodium acetate gave *3′-bromo-3,5-di-iodo-*D*-thyronine* (3·23 g., 94%), m. p. 247—249° (decomp.), $[\alpha]_D^{20}$ −25·6° (Found: C, 29·8; H, 2·0; Hal, 55·25; N, 2·3. $C_{15}H_{12}BrI_2NO_4$ requires C, 30·1; H, 2·1; Hal, 54·6; N, 1·9%). This material contained <2% each of di-iodo- and dibromodi-iodo-thyronine.

*3′,5′-Dibromo-3,5-di-iodo-*D*-thyronine.*—3,5-Di-iodo-D-thyronine, treated as in the last experiment with bromine (2·73 g.) for 80 hr., gave *3′,5′-dibromo-3,5-di-iodo-*D*-thyronine* (3·66 g., 94%), m. p. 246° (decomp.), $[\alpha]_D^{20}$ −21·0° (Found: C, 27·0; H, 1·8; Hal, 60·0; N, 2·2. $C_{15}H_{11}Br_2I_2NO_4$ requires C, 26·4; H, 1·6; Hal, 60·6; N, 2·05%). This material contained 3% of 3′-bromo-3,5-di-iodo-D-thyronine.

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GLAXO LABORATORIES, LTD.,
GREENFORD, MIDDLESEX.

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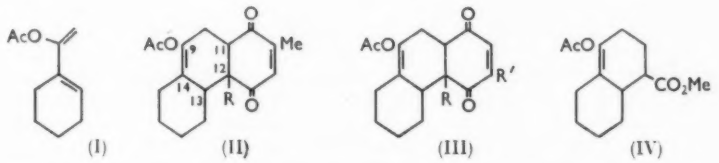
557. *Reduced Cyclic Compounds. Part XII.* Further Diels–Alder Reactions of 1-1′-Acetoxyvinylcyclohexene.*

By M. F. Ansell and B. A. Knights.

The Diels–Alder reaction of 1-1′-acetoxyvinylcyclohexene with toluquinone, 2,5-xyloquinone, and 6- and 5-methoxytoluquinone are reported. Except in the last case the structures of the products obtained were determined. The aromatisation of certain Diels–Alder adducts in boiling methanol is reported.

The recorded [1,2] Diels–Alder reactions of 1-1′-acetoxyvinylcyclohexene (I) include only one example,[1] 2,6-xyloquinone, of the use of an unsymmetrically substituted *p*-benzoquinone as a dienophil. We now report the reaction of this diene with toluquinone, 2,5-xyloquinone, and 5- and 6-methoxytoluquinone.

The diene (I) reacted with toluquinone exclusively at the unsubstituted double bond, to give a mixture of the adducts (II; R = H) and (III; R = H, R′ = Me). The structure of the former was established by reduction with lithium aluminium hydride (two reductions were necessary; cf. ref. 1), followed by dehydration and dehydrogenation to 2-methylphenanthrene. The ultraviolet spectrum of this adduct had its main maximum at 240 mμ, which is identical with the main maximum [1] for the compound (III; R = R′ = Me), an ene-dione of the same substitution type. The second adduct (III; R = H, R′ = Me) was not obtained pure, but its structure was shown by degradation to 3-methylphenanthrene.



(I) (II) (III) (IV)

The reaction between 2,5-xyloquinone and 1-1′-acetoxyvinylcyclohexene yielded a homogeneous product which was shown by degradation to 2-methylphenanthrene to be 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-2,12-dimethylphenanthrene (II; R = Me). Thus 2,5-xyloquinone and, as previously reported,[1] 2,6-xyloquinone react with the acetoxy-diene (I) to yield only adducts containing an angular methyl group at $C_{(12)}$. The factors controlling this specificity are not clear. From simple polarity considerations, in which $C_{(2)}$ of the diene is positively charged, a conclusion consistent with its known [2c,e] reaction with methyl acrylate to yield the bicyclic ester (IV), both xyloquinones would be expected to yield products containing an 11-methyl group. If (i) we expect the maximum accumulation of unsaturation in the transition state,[3] (ii) a methyl group is considered as more unsaturated than hydrogen,[4] and (iii) the diene and the xyloquinones react by *endo*-addition, then the substituent on the non-reacting ene-dione system would be expected to influence the structure of the product by its interaction with the enol-acetate moiety. Thus neither of the two principles used in predicting the course of the Diels–Alder reaction is applicable in these cases. The principle of maximum accumulation of unsaturation is also violated

* Part XI, *J.*, 1961, 206.

[1] Ansell and Brooks, *Chem. and Ind.*, 1955, 916; *J.*, 1956, 4518.

[2] (*a*) Nazarov, Kucherov, Andreyv, and Segal, *Doklady Akad. Nauk S.S.S.R.*, 1955, **104**, 729; (*b*) Nazarov, Kucherov, and Segal, *Bull. Acad. Sci. U.S.S.R.*, 1956, 1241 (U.S. translation); (*c*) Nazarov, Kucherov, and Andreev, *ibid.*, 1957, 345; (*d*) Nazarov, Kucherov, Andreev, and Segal, *Proc. Acad. Sci. (U.S.S.R.)*, 1958, **119**, 277 (U.S. translation); (*e*) Winternitz and Balmossiere, *Tetrahedron*, 1958, **2**, 100; (*f*) Bergmann and Becker, *J. Amer. Chem. Soc.*, 1959, **81**, 221.

[3] Alder and Stein, *Angew. Chem.*, 1937, **50**, 510; Alder and Windemuth, *Ber.*, 1938, **71**, 1948.

[4] Cf. Alder and Vogt, *Annalen*, 1949, **564**, 120.

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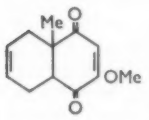
in the addition of methyl acrylate to the acetoxy-diene (I). This is attributed [2c] to interaction of the enol-acetate group of the diene with the methoxycarbonyl group of the dienophil.

Condensation of the diene (I) with 6-methoxytoluquinone (Me = 2) resulted in exclusive formation of the adduct (III; R = Me, R′ = MeO) whose ultraviolet spectrum had its main maximum at 272 mμ, similar to that [5] (269 mμ) for the compound (V), indicating that addition had occurred at the methyl-ethene linkage, as was proved by the following degradation. Methanolysis of the adduct (III; R = Me, R′ = OMe) gave the triketone (VI), which after ozonolysis, followed by oxidation with hydrogen peroxide and Clemmensen reduction, gave the acid (VII). This acid was dehydrogenated with concomitant decarboxylation to 1-methylnaphthalene.

In contrast to the specificity of the reaction of 6-methoxytoluquinone with the diene (I), 5-methoxytoluquinone afforded a complex mixture. Three products were isolated by chromatography and fractional crystallisation, each having the analysis of a normal adduct and a maximum in its ultraviolet absorption spectrum consistent with a methoxy-substituted ene-dione system. None of these compounds was obtained in amount sufficient for its structure to be established. The presence of other products, possibly modified adducts, was inferred from the light-absorption characteristics of the unresolved mixtures.

The reaction between 1-1′-acetoxyvinylcyclohexene (I) and 2,6-xyloquinone is reported [1] to give a greater yield in ethanol than in benzene. A similar effect was observed with this diene and 5-methoxytoluquinone, which did not react in boiling benzene during



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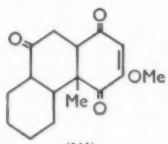

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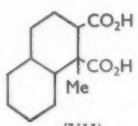
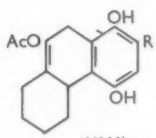
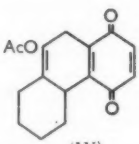


(VII)



(VIII)



(IX)

96 hr.; this is in contrast to the recorded [5] addition of 6-methoxytoluquinone to butadiene at *ca.* 105°. When, however, toluquinone and the diene (I) were allowed to react in methanol the only isolable product was the quinol (VIII; R = Me), which was also formed when a methanolic solution of the normal adduct (II; R = H) was boiled. The reaction between the diene and benzoquinone in ethanol yields [2e] the adduct (III; R = R′ = H) in a 63% yield after 72 hr. at room temperature, but the yield falls to 30% if the solution is boiled for 5 hr. and then left overnight; we have found that the initial reaction in methanol solution afforded the expected adduct (III; R = R′ = H) after a short reaction time, but on prolonged heating the aromatic compound (VIII; R = H) together with the related quinone (IX) was formed. Aromatisation of the ene-dione (III; R = R′ = H) also occurs at (or above) its melting point, for it is reported [1,2e] that this compound melts initially at 118—120°, resolidifies at *ca.* 155°, and melts again at *ca.* 225° [the quinol (VIII; R = H) has m. p. 228—231°]. Previous cases of aromatisation of ene-diones fall into two classes; those [6] in which the reaction is catalysed by alkali or mineral acid and those [6b,7] in which the ene-dione is heated alone or in water or acetic acid. Aromatisation under the mild conditions of boiling methanol has not been previously reported, although partial enolisation of the ketone (V) on recrystallisation from methanol is recorded (ref. 5, footnote 14).

[5] Woodward, Sondheimer, Taub, Hensler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.
[6] *Inter al.*, (*a*) Fieser and Chang, *J. Amer. Chem. Soc.*, 1942, **64**, 2043; (*b*) Tomayo and Leon, *J.*, 1948, 1499; (*c*) Robins and Walker, *J.*, 1952, 642.
[7] *Inter al.*, Ostrozhinskaya, *Zhur. obshchei Khim.*, 1946, **16**, 1053.

Experimental

Ultraviolet absorption spectra were measured for 96% ethanol solutions unless otherwise stated.

Reaction of 1-1′-*Acetoxyvinylcyclohexene with Toluquinone.*—A solution of 1-1′-acetoxyvinylcyclohexene (20 g.) and toluquinone [8] (12·2 g.) in benzene (150 ml.) was kept at room temperature for 4 days. Most of the benzene was then removed under reduced pressure and light petroleum (b. p. 40—60°) was added to the warm residue until the mixture was just cloudy. This solution, on cooling, deposited crude 9-*acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-2-*methyl*-1,4-*dioxophenanthrene* (II; R = H) (7·8 g.), m. p. 123—134°. Recrystallisation from benzene–light petroleum (b. p. 60—80°) gave the pure compound, m. p. 136—139·5°, $\lambda_{max.}$ (in hexane) 240, 359 mμ (log ε 4·07, 1·78), $\lambda_{infl.}$ 284 mμ (log ε 1·97) (Found: C, 70·8; H, 7·0. $C_{17}H_{20}O_4$ requires C, 70·85; H, 6·9%). Concentration of the mother-liquors from the first crystallisation gave material (12·6 g.), m. p. 95—120°, which on fractional crystallisation from methanol yielded a further quantity (2·5 g.) of the above adduct, m. p. 134—138°, and an impure sample (3·1 g.), m. p. 113—123°, of 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-1,4-dioxo-3-methylphenanthrene.

Degradation of 9-*Acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-2-*methyl*-1,4-*dioxophenanthrene.*—The compound (0·023 mole) was added *via* a Soxhlet extraction apparatus (3·5 hr. required) to a stirred suspension of lithium aluminium hydride (4·0 g.) in dry ether (300 ml.). After cooling, water was cautiously added and the ethereal solution decanted from the precipitated solids which were washed with ether. The residue left on evaporation of the dried ($MgSO_4$) ethereal solutions contained ketonic material (that formed a 2,4-dinitrophenylhydrazone) and was dissolved in ether (75 ml.) and added to a suspension of lithium aluminium hydride (4·0 g.) in ether (200 ml.). After being boiled for 6 hr., this mixture was worked up as before. The resulting non-ketonic material (5·0 g.) was dehydrated at 180° for 45 min., in a stream of nitrogen, with powdered fused potassium hydrogen sulphate (5 g.). After addition of water the product was extracted with ether and dried (K_2CO_3). The solvent was then removed and the residue (4 g.) heated with 5% palladium–charcoal (2 g.) at 290° ±5° for 2 hr. The organic product (extracted with benzene) was chromatographed in light petroleum (b. p. <40) on alumina (Peter Spence, type H) to yield 2-methylphenanthrene (1 g.), m. p. and mixed m. p. 55—57°. The derived picrate had m. p. 118·5—120°. Haworth [9] records m. p. 55—56° (picrate, m. p. 118—119°).

Degradation of 9-*Acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-3-*methyl*-1,4-*dioxophenanthrene.*—This compound (0·016 mole) was degraded as in the previous experiment except that the dehydrogenation was effected in boiling diphenylamine for 20 hr. The cooled mixture was extracted with ether; the ethereal solution was filtered and saturated with dry hydrogen chloride. The precipitated diphenylamine hydrochloride was filtered off, the filtrate evaporated, and the residue chromatographed in light petroleum (b. p. <40°) on alumina to yield a colourless oil from which was derived 3-methylphenanthrene picrate, m. p. 135—137° undepressed in admixture with an authentic specimen,[1] m. p. 138—139·5°.

9-*Acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-2,12-*dimethyl*-1,4-*dioxophenanthrene.*—A solution of 1-1′-acetoxyvinylcyclohexene (12 g.) and 2,5-xyloquinone * (8·5 g.) in ethanol (200 ml.) was boiled under reflux for 40 hr. and the solvent then removed under reduced pressure. After treatment of the residue with light petroleum (b. p. 40—60°) the solid product was filtered off and washed with a little ether, to yield 9-*acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-2,12-*dimethyl*-1,4-*dioxophenanthrene* (II; R = Me) (8·8 g., 46%), m. p. 154—158°. Recrystallisation from ethanol gave the pure adduct as needles, m. p. 157—159°, $\lambda_{max.}$ 243, 352 mμ (log ε 3·87, 2·41) (Found: C, 71·6; H, 7·3. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%).

Degradation of 9-*Acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-2,12-*dimethyl*-1,4-*dioxophenanthrene.*—Degradation of this compound (0·023 mole) was effected as for 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-2-methyl-1,4-dioxophenanthrene except that the final dehydrogenation was carried out with selenium (12 g.) at 320—350° for 20 hr. Distillation at <190°/0·1 mm. of the organic dehydrogenation product afforded a pale yellow oil (0·8 g.) from which was obtained 2-methylphenanthrene

* Obtained in low yield by the oxidation of 2,5-xylidine as described [8] for oxidation of *o*-toluidine.

[8] Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Co. Ltd., London, 1957, p. 423.

[9] Haworth, *J.*, 1932, 1125.

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picrate, m. p. 116—119°, which was not depressed in admixture with an authentic specimen of m. p. 118—119°.

9-*Acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-3-*methoxy*-12-*methyl*-1,4-*dioxophenanthrene*.—A solution of 6-methoxytoluquinone (15 g.) and 1-1′-acetoxyvinylcyclohexene (22 g.) in methanol (500 ml.) was heated under reflux for 73 hr. and the solvent then evaporated (reduced pressure). Ether was added to the residue, and the solid product was filtered off and washed with a little ether, to yield 9-*acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-3-*methoxy*-12-*methyl*-1,4-*dioxophenanthrene* (III; R = Me, R′ = OMe) (26 g., 82%), m. p. 178—188°. Recrystallisation from ethanol gave colourless octahedra (24 g.), m. p. 185—190°, $\lambda_{max.}$ 272 mμ (log ε 3·91), whose m. p. was not improved on further crystallisation (Found: C, 68·1; H, 7·0. $C_{18}H_{22}O_5$ requires C, 67·9; H, 7·0%)

Δ^2-*Dodecahydro*-3-*methoxy*-12-*methyl*-1,4,9-*trioxophenanthrene*.—A solution of 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-3-methoxy-12-methyl-1,4-dioxophenanthrene (35 g.) in anhydrous methanol (1 l.) containing 98% sulphuric acid (12 ml.) was boiled for 30 min., then concentrated to *ca.* 250 ml. under reduced pressure and cooled. The precipitated crystals were filtered off and washed with a little methanol, to give Δ^2-*dodecahydro*-3-*methoxy*-12-*methyl*-1,4,9-*trioxophenanthrene* (VI) (14·1 g.), m. p. 195—197°, which on recrystallisation from methanol–chloroform gave the triketone (11 g.), m. p. 207—212°, $\lambda_{max.}$ 275 mμ (log ε 3·92). The analytical sample had m. p. 209·5—214·5° (Found: C, 69·6; H, 7·4. $C_{16}H_{20}O_4$ requires C, 69·6; H, 7·3%). This material showed no infrared absorption at 5·7—5·75 μ, indicating the absence of the enol-acetate group.

Degradation of Δ^2-*Dodecahydro*-3-*methoxy*-12-*methyl*-1,4,9-*trioxophenanthrene*.—A solution of the triketone (11 g.) in acetic acid (110 ml.) and chloroform (110 ml.) was treated with ozonised air for 12 hr. Water (12 ml.) and 30% hydrogen peroxide were then added and the solution was boiled for 30 min. The chloroform and most of the acetic acid were removed by steam-distillation, and the residual solution, when cooled, deposited starting material (1·4 g.) which was filtered off. The filtrate was made alkaline with sodium carbonate and extracted with ether. Sodium hydroxide (15 g.) and 30% hydrogen peroxide (100 ml.) were added to the aqueous phase, and the mixture was boiled for 10 min. The hot brown solution was decolorised by the addition of 30% hydrogen peroxide (*ca.* 30 ml.), then acidified with hydrochloric acid and extracted with ether. The residue (8 g.) obtained on evaporation of the ether extract was dissolved in toluene (150 ml.) and acetic acid (60 ml.), and the mixture together with amalgamated zinc wool (90 g.), hydrochloric acid (150 ml.), and water (60 ml.) was heated under reflux for 24 hr. Further additions (3 × 60 ml.) of hydrochloric acid were made during this time. The toluene and most of the acetic acid were removed by steam-distillation and the aqueous solution was decanted from the zinc. This solution, on cooling, deposited an acidic solid which was filtered off and twice recrystallised from benzene–ethanol to yield *perhydro*-1-*methylnaphthalene*-1,2-*dicarboxylic acid* (VII) (0·7 g.), m. p. 203—209·5° (Found: C, 65·4; H, 8·7. $C_{13}H_{20}O_4$ requires C, 65·0; H, 8·4%).

This solid together with 10% palladium–charcoal (0·8 g.) and acetone (14 ml.) was heated in a metal tube at 350° for 12 hr. The resulting solution was filtered and evaporated and the residual oil chromatographed in light petroleum (b. p. 30—40°) on alumina. Vapour-phase chromatography of the eluted oil at 150° on a " Pye Argon Chromatograph " with Apiezon " L " as the stationary phase showed it to be almost entirely 1-methylnaphthalene (1- and 2-methylnaphthalene are separable under these conditions). This result was confirmed by the infrared spectrum of the eluted oil which was essentially that of 1-methylnaphthalene.

Reaction of 1-1′-*Acetoxyvinylcyclohexene with* 5-*Methoxytoluquinone*.—This reaction was carried out as for the analogous reaction of 6-methoxytoluquinone, the reaction time being 96 hr. The use of benzene as a solvent (96 hr./b. p.) afforded only unchanged quinone. Thus was obtained material (A) (17 g.), m. p. 125—135°. Crystallisation from ether of the residue obtained on evaporation of the filtrate at 100°/1 mm. gave material B (2·5 g.), m. p. 125—135° (some sintering at 80—100°). Chromatography, in ether–benzene on silica gel, of the residue from the crystallisation of (B) gave several fractions (C) (2·3 g.). Recrystallisation of (A) from methanol yielded: (D) (2·4 g.), m. p. 145—172° (mainly quinone); (E) (7·0 g.), m. p. 135—164° (contaminated with quinone); and (F) (3·6 g.), m. p. 126—195°. Extraction (Soxhlet) of (E) with boiling water (to remove quinone) followed by recrystallisation from methanol gave an *adduct* (white prisms), m. p. 164—165°, $\lambda_{max.}$ 274 mμ (log ε 3·96) (Found: C, 67·8; H, 6·7. $C_{18}H_{22}O_5$ requires C, 67·9; H, 7·0%). Recrystallisation of the fractions (C) from methanol

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afforded another *adduct* (yellow prisms), m. p. 176—181°, $\lambda_{max.}$ 272 mμ (log ε 4·04) (Found: C, 68·3; H, 7·1; OMe, 10·1%; *M*, 308. $C_{18}H_{22}O_5$ requires C, 67·9; H, 7·0; OMe, 9·75%; *M*, 318), together with a third *adduct* (300 mg.) (stout plates from methanol), m. p. 172—175°, $\lambda_{max.}$ 271 mμ (log ε 4·04) (Found: C, 68·3; H, 6·8. $C_{18}H_{22}O_5$ requires C, 67·9; H, 7·0%). The " second " adduct was also obtained (2·5 g. in all) by recrystallisation of material (B) from benzene.

The mixture (F) had $\lambda_{max.}$ 252 mμ, 336—342 mμ (log ε 3·66, 3·43). Its infrared spectrum showed strong absorption at 5·76 (enol acetate), 6·24 (double bond of enol ether), 6·4 (conjugated polyene), and *ca.* 3·3br (OH) but only weak absorption at 5·85, 6·00, and 6·08 μ (C=O region). This suggests the presence of an enolic compound, possibly 10-acetoxy-1,2,3,4-tetrahydro-5,8-dihydroxy-7-methoxy-13-methylphenanthrene.

Reaction of 1-1′-*Acetoxyvinylcyclohexene with Benzoquinone.*—A solution of *p*-benzoquinone (2·2 g., 0·02 mole) and 1-1′-acetoxyvinylcyclohexene (3·5 g., 0·021 mole) in anhydrous methanol (30 ml.) was boiled for 2 hr., then cooled, and light petroleum (b. p. 30—40°) (30 ml.) was added. This solution, when left overnight at 0°, deposited 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-1,4-dioxophenanthrene (1·8 g., 32%), m. p. 106—120°, raised to 117—120° (lit.,[1] 118—120°) on recrystallisation from ether.

This experiment was repeated, but with a reaction time of 18 hr., after which time the solvent was removed under reduced pressure and a mixture of light petroleum (b. p. 40—60°) (20 ml.) and ethanol (10 ml.) was added. The precipitate was filtered off and washed with a little ethanol, to yield 10-*acetoxy*-1,2,3,4,9,12-*hexahydro*-5,8-*dihydroxyphenanthrene* (VIII; R = H) (1·9 g., 34%), m. p. 196—220°. Repeated recrystallisation from benzene–ethanol raised the m. p. to 228—231° [$\lambda_{max.}$ 292 mμ (log ε 3·36)] (Found: C, 69·7; H, 6·55. $C_{16}H_{18}O_4$ requires C, 70·1; H, 6·6%). Slow evaporation of the mother-liquors deposited 9-*acetoxy*-5,6,7,8,10,13-*hexahydro*-1,4-*phenanthraquinone* (IX) (1 g.) as yellow needles, m. p. 135—142°. Recrystallisation raised the m. p. to 137—145° [$\lambda_{max.}$ 250, 350—355 mμ (log ε 3·95, 2·81)] which was not further improved by repeated crystallisation (Found: C, 70·7; H, 5·8. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

10-*Acetoxy*-1,2,3,4,9,12-*hexahydro*-5,8-*dihydroxy*-7-*methylphenanthrene.*—A solution of 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-2-methyl-1,4-dioxophenanthrene (1·8 g) in methanol (50 ml.) was boiled for 18 hr. and the solvent then removed at reduced pressure. The semisolid residue was extracted with benzene, and the nearly insoluble 10-*acetoxy*-1,2,3,4,9,12-*hexahydro*-5,8-*dihydroxy*-7-*methylphenanthrene* (VIII; R = Me) (1 g. 55%), m. p. 200—205° (decomp.), was collected. Recrystallisation from benzene–ethanol gave the pure compound, m. p. 207—212°, $\lambda_{max.}$ 289 mμ (log ε 4·35) (Found: C, 70·5; H, 7·0. $C_{17}H_{20}O_4$ requires C, 70·85; H, 7·0%). This same compound was also isolated after reaction between toluquinone and 1-1′-acetoxyvinylcyclohexene in boiling methanol.

The authors are indebted to the University of London Central Research Fund and the Royal Society for financial assistance and to the Governors of Queen Mary College for an award (to B. A. K.).

Queen Mary College (University of London),
Mile End Road, London, E.1.

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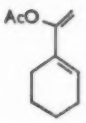
558. *Reduced Cyclic Compounds. Part XIII.* The Reaction of 1-1′-Acetoxyvinylcyclohexene with p-Benzoquinones containing a Methoxycarbonyl Group.†*

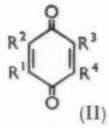
By M. F. Ansell and G. C. Culling.

The Diels–Alder reactions of 1-1′-acetoxyvinylcyclohexene with methoxycarbonyl- and 2,5-dimethoxycarbonyl-benzoquinone and 6-methoxycarbonyl- and 6-methoxy-3-methoxycarbonyl-tolu-1,4-quinone are reported. In each case the product contained an angular methoxycarbonyl group. Some comments are made on the Diels–Alder reactions of substituted *p*-benzoquinones. An attempted preparation of the 2,5-dimethoxycarbonyl-quinone is described.

An unsymmetrically substituted *p*-benzoquinone may undergo the Diels–Alder reaction, preferentially or exclusively, at either of the double bonds, the nature of the substituents being the determining factor. For the addition of buta-1,3-diene to such quinones Orchin and Butz[1] formulated the following hypothesis: "Butadiene reacts faster with carbon atoms attached to hydrogen than to others (steric effect) and of these as an anionoid reagent it reacts fastest with the most cationoid carbon in the quinone (electrostatic effect)." As these authors point out, this hypothesis satisfactorily explains the addition of butadiene to the methoxycarbonyl-ethene linkage of the quinone (IIa), but does not explain the addition at the methyl-ethene linkage of the quinone (IIb) unless it is assumed that the steric effect of a methoxy-group is greater than that of a methyl group. However, we considered that the order of dienophilic activity observed with these quinones, namely, methoxycarbonyl-ethene > methyl-ethene > methoxy-ethene is explicable if the dienophilic activity of the ethene linkage depends on whether its electron-density is greater or less than that of the ethene linkage in benzoquinone. Thus the lower the electron-density the greater the reactivity of the ethene linkage. The Diels–Alder reactions of monosubstituted benzoquinones in which the substituent is electron-donating, have been shown to occur at the unsubstituted ethene linkage, in accord with the views of Orchin and Butz and of ourselves. However, if the substituent is an electron-attracting group such as confers dienophilic properties on an olefin, we consider that, in contrast to the first part of Orchin and Butz's hypothesis, the reaction should occur at the substituted ethene linkage. The Diels–Alder reactions of such quinones have never been investigated.



(I)



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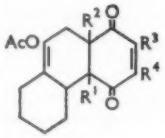


(III)

a: $R^1 = CO_2Me$, $R^2 = R^3 = H$, $R^4 = Me$.
b: $R^1 = H$, $R^2 = Me$, $R^3 = OMe$, $R^4 = H$.
c: $R^1 = CO_2Me$, $R^2 = R^3 = R^4 = H$.
d: $R^1 = CO_2Me$, $R^2 = Me$, $R^3 = OMe$, $R^4 = H$.
e: $R^1 = Me$, $R^2 = CO_2Me$, $R^3 = H$, $R^4 = OMe$.

f: $R^1 = CO_2Me$, $R^2 = R^3 = H$, $R^4 = Me$.
g: $R^1 = CO_2Me$, $R^2 = R^3 = Me$, $R^4 = H$.
h: $R^1 = CO_2Me$, $R^2 = H$, $R^3 = CO_2Me$, $R^4 = H$.
i: $R^1 = R^2 = R^3 = R^4 = H$.

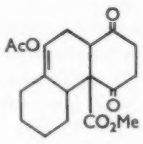
We now report, as a continuation of another investigation,[2] the Diels–Alder reaction of 1-1′-acetoxyvinylcyclohexene (I) with methoxycarbonylbenzoquinone (IIc), 6-methoxy-3-methoxycarbonyl-1,4-toluquinone (IId), and 6-methoxycarbonyl-1,4-toluquinone (IIf), to

* Part XII, preceding paper. † For a preliminary communication see ref. 3.

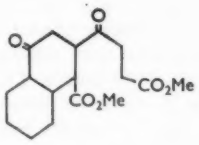
[1] Orchin and Butz, *J. Org. Chem.*, 1943, **8**, 509.
[2] (*a*) Ansell and Brooks, *J.*, 1956, 4518; (*b*) Ansell and Knights, preceding paper.

form the adducts (IIIc), (IIId or e), and (IIIf) respectively, each containing an angular ester group. The adducts (IIIc) and (IIId or e) constitute the first two examples of addition of a diene to the more substituted ethene linkage of a benzoquinone. These results are not explicable on the hypothesis of Orchin and Butz (should this be applicable to dienes in general), but are consistent with our view that addition of the diene occurs at the more electron-deficient ethene-linkage of the quinone provided that there is no steric opposition to such a reaction. In these two examples the activation of the ethene linkage by the methoxycarbonyl group overcomes any steric factors operating against addition of the diene to the more substituted ethene linkage. That steric factors do operate in such reactions has been shown [3] by addition of the acetoxy-diene (I) to the monosubstituted ethene linkage of the quinone (IIg).

Adding methoxycarbonylbenzoquinone (IIc) to 1-1′-acetoxyvinylcyclohexene (I) caused a spontaneous exothermic reaction which formed 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-12-methoxycarbonyl-1,4-dioxophenanthrene (IIIc) in a 97% yield. That addition had occurred at the methoxycarbonyl-ethene linkage was suggested by the ultraviolet spectrum of the adduct which showed an absorption maximum at 225 mμ, identical with that of the adduct (IIIi) from *p*-benzoquinone, and was confirmed when the product was not aromatised under conditions which aromatise the simple adduct (IIIi); further, the nuclear magnetic resonance spectrum indicated the presence of two vinyl-hydrogen atoms (τ 3·215, 3·179) as well as an enol acetate (τ 7·859) and a methoxycarbonyl group (τ 6·180). Supporting evidence was reduction of the adduct by potassium borohydride to a mixture of isomeric triols which on dehydration and dehydrogenation by palladium afforded phenanthrene. If the methoxycarbonyl group had been non-angular the product could have been 2- or 3-methoxycarbonylphenanthrene. It was expected from a consideration of the polarities of the diene and dienophil, the structure of the adduct from the acetoxy-diene (I) and 6-methoxycarbonyltoluquinone (IIf) (see below), and from the structure [4] of the adduct from the same diene and methyl acrylate, that the methoxycarbonyl group would be attached to $C_{(12)}$ and not $C_{(11)}$. This was confirmed by the following degradation. The benzoquinone adduct (IIIc) was reduced with zinc and acetic acid to its dihydro-derivative (IV) (a β-keto-ester) which was treated with sodium methoxide in anhydrous methanol. The product contained both neutral and acidic material, the latter arising by alkyl–oxygen fission under these conditions.[5] The product at this stage was expected to be the compound (V) (or the derived acid) and was subjected to Clemmensen reduction followed by esterification and dehydrogenation. It was hoped to isolate the diester (VI). However,



(IV)



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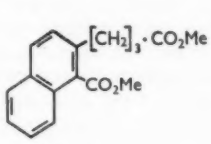
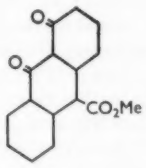


(VI)



(VII)

the product was anthracene, produced by cyclisation of the keto-ester (V) to the perhydroanthracene derivative (VII), which by the subsequent procedure yielded anthracene. This unexpected result confirms our view that the ester group is attached at $C_{(12)}$ in the original adduct. The intermediate (V) could arise if the ester group was attached at position 3, but the previous evidence is against this. An adduct containing the ester group either at position 11 or 2 could not give anthracene by a rational sequence of reactions.

[3] Ansell, Culling, Nash, Wilson, and Lown, *Proc. Chem. Soc.*, 1960, 405.
[4] Winternitz and Balmossiere, *Tetrahedron*, 1958, **2**, 100.
[5] Cf. Bunnett, Robinson, and Pennington, *J. Amer. Chem. Soc.*, 1950, **72**, 2378.

6-Methoxycarbonyltoluquinone (IIf) reacted readily with the acetoxy-diene (I) to yield 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-12-methoxycarbonyl-3-methyl-1,4-dioxophenanthrene (IIIf). The ultraviolet absorption spectrum of the latter had a maximum at 243 mμ, indicating (cf. ref. 2) the presence of a methyl-substituted ene-dione system. The adduct (IIIf) was reduced with potassium borohydride to a mixture of triols, and then dehydrogenated by palladium or selenium to 3-methylphenanthrene, thus confirming its structure.

It is known [2b] that 5- and 6-methoxytoluquinone react with the acetoxy-diene (I) at the methyl-ethene linkage. This we consider (see above) to be due to the deactivating effect of the methoxy-group. We therefore considered that 6-methoxy-3-methoxycarbonyltoluquinone (IId) would undergo the Diels–Alder reaction at the more substituted ethene linkage. The quinone (IId) was prepared by oxidation of the known [6] parent quinol, and unlike the previous methoxycarbonylquinones is stable. It (IId) reacted slowly with acetoxy-diene, only a 39% yield of adduct (IIId or e) being obtained after 60 hr. at 100°. That addition had occurred at the disubstituted ethene linkage was shown by the adduct's having a maximum at 278 mμ in its ultraviolet absorption spectrum, indicative [2b] of a methoxy-substituted ene-dione system, and from its nuclear magnetic resonance spectrum, which showed the presence of one vinyl-hydrogen atom (τ 4·101) besides the angular methyl group (τ 8·833), the enol-acetate group (τ 7·817), the methoxy-group (τ 6·3505), and the methoxycarbonyl group (τ 6·173). Decision between the possible structures (IIId) and (IIIe) is under investigation, but structure (IIIe) is considered the more probable. This is the second example of the addition of a diene to the more substituted side of a substituted *p*-benzoquinone.

At one stage in our studies we wished to ascertain the ultraviolet absorption maximum associated with the methoxycarbonyl-enedione system. Such a system would be found in the monoadduct from the acetoxy-diene (I) and a quinone such as 2,5-dimethoxycarbonylbenzoquinone (IIh). Dimethyl 2,5-dihydroxyterephthalate was prepared by dehydrogenation of dimethyl 2,5-dioxocyclohexane-1,4-dicarboxylate with bromine; the ethyl ester has been similarly prepared.[7] This quinol, like the diethyl ester, was bright yellow (many aromatic *o*-hydroxy-carbonyl compounds are coloured [8]) and exhibited a blue fluorescence in benzene solution. Its structure was confirmed by conversion into the known [9] diacetate (colourless). An attempted oxidation of this quinol with oxides of nitrogen [10] yielded dimethyl 2,5-dihydroxy-3,6-dinitroterephthalate, even at 0° in the presence of anhydrous potassium carbonate with the oxides of nitrogen dried over potassium carbonate. The structure of this product was proved by its infrared spectrum and its analysis and that of its diacetate. Oxidation of dimethyl 2,5-dihydroxyterephthalate with silver oxide gave a mixture of the unchanged quinol and the red quinhydrone, the latter being obtained even when a large excess of freshly prepared oxide was used for a long time. The infrared spectra of the quinhydrone and 2,3-dimethoxycarbonylbenzoquinone [11] both have two peaks (5·79 and 6·01 μ) in the carbonyl region. A weak peak at 3·0 μ (OH) in the spectrum of the quinhydrone is not surprising as the weak and broad absorption in this region of the parent quinol would be further broadened by the effect of hydrogen-bonding [12] and weakened by the dilution effect of the quinone portion of the quinhydrone. The assignment of the quinhydrone structure was confirmed by estimation [13] of its quinone content, and by the fact that solutions of the red quinhydrone, in ether or benzene, were yellow, as could be explained by its dissociation in solution. However, when the material was warmed with methanol it was reduced to the yellow

[6] Aghoramurithy and Seshadri, *Proc. Indian Acad. Sci.*, 1952, 327.
[7] Herrmann, *Annalen*, 1882, **211**, 327.
[8] Smith and Thomson, *J.*, 1960, 346.
[9] Bernatek and Thorensen, *Acta Chem. Scand.*, 1955, **9**, 743.
[10] Cf. Brook, *J.*, 1952, 5040.
[11] Ansell and Wilson, unpublished observation.
[12] Fox and Martin, *Proc. Roy. Soc.*, 1937, **162**, *A*, 419.
[13] Hickinbottom, "Reactions of Organic Compounds," Longman, Green & Co., Ltd., London, 1957, p. 288.

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quinol. Further, the quinhydrone reacted with the acetoxy-diene (I) to yield dimethyl 2,5-dihydroxyterephthalate together with an adduct. The latter was also obtained when dimethyl 2,5-dihydroxyterephthalate was oxidised by silver oxide in the presence of the diene. The analysis of the adduct indicated that it was a bis-adduct, from two molecules of the diene and one of the quinone, and, in agreement, its ultraviolet spectrum showed no ene-dione absorption in the region 200—350 mμ.

Experimental

Ultraviolet absorption spectra are recorded for ethanol solutions.

9-Acetoxy-Δ$^{2,9(14)}$-decahydro-12-methoxycarbonyl-1,4-dioxophenanthrene (IIIc).—Methoxycarbonylbenzoquinone [14] (IIc) (2·6 g., 0·016 mole) was added to 1-1′-acetoxyvinylcyclohexene [22] (I) (3·0 g., 0·018 mole) containing a crystal of quinol. An exothermic reaction ensued and the mixture was cooled. Dry benzene (10 ml.) was added and the mixture left overnight. The solvent was removed under reduced pressure, and the residue triturated with light petroleum (b. p. 60—80°), to yield *9-acetoxy-Δ$^{2,9(14)}$-decahydro-12-methoxycarbonyl-1,4-dioxophenanthrene* (IIIc) (5·0 g., 97%), orange, m. p. 100—115°. Crystallisation from methanol gave the pure compound, m. p. 128·5—130°, $\lambda_{max.}$ 225 mμ (log ε 4·02), 5·71 (enol-acetate), 5·80 (ester), 5·90 and 5·95 μ (αβ-unsaturated C=O) (Found: C, 64·8; H, 6·2. $C_{18}H_{20}O_6$ requires C, 65·0; H, 6·0%). When the adduct was treated as in the following experiment, 90% of it was recovered.

Aromatisation of 9-Acetoxy-Δ$^{2,9(14)}$-decahydro-1,4-dioxophenanthrene (IIIi).—48% Hydrobromic acid (1 drop) was added to a solution of the dioxo-phenanthrene [23] (0·5 g.) in glacial acetic acid (3 ml.) at 90°. After 10 min. a precipitate was formed which, after 1 hr., was filtered off and washed with acetic acid to yield 10-acetoxy-1,2,3,4,9,12-hexahydro-5,8-dihydroxyphenanthrene (0·4 g.), m. p. 185—195° (decomp.). Recrystallisation from acetic acid gave the pure compound, m. p. 226—230° (decomp.) (lit.,[23b] 228—231°).

9-Acetoxy-Δ$^{9(14)}$-dodecahydro-12-methoxycarbonyl-1,4-dioxophenanthrene (IV).—Zinc powder (60 g.) was added to 9-acetoxy-Δ$^{2,9(14)}$-decahydro-1,4-dioxophenanthrene (IIIc) (30 g.) in acetic acid (400 ml.), and the mixture was stirred and heated on a steam-bath for 16 hr., then cooled and filtered. Trituration, with dry methanol (100 ml.), of the residue obtained on evaporation of the filtrate under reduced pressure gave *9-acetoxy-Δ$^{9(14)}$-dodecahydro-12-methoxycarbonyl-1,4-dioxophenanthrene* (IV) (28 g., 93%), m. p. 179—183°. The analytical sample (from methanol) had m. p. 185—186° (Found: C, 64·7; H, 6·7. $C_{18}H_{22}O_6$ requires C, 64·8; H, 6·6%). The double-bond peak (6·22 μ) in the infrared spectrum of the starting material was absent from the spectrum of the reduced material.

Degradation of the Dihydro-derivative (IV) *to Anthracene.*—The dihydro-derivative (IV) (20 g.) was dissolved in oxygen-free sodium methoxide (from sodium, 2·4 g.) in methanol (120 ml.) at 5°, left at room temperature for 14 hr., and then boiled under reflux (nitrogen) for 15 min. The cool, brown mixture was poured on ice and 4N-sulphuric acid and extracted with ether. The product was separated into acidic and non-acidic material in the usual way. The non-acidic material (7 g.) was discarded. A mixture of acidic material (10 g.), amalgamated zinc wool (40 g.), water (30 ml.), concentrated hydrochloric (70 ml.), toluene (40 ml.), and glacial acetic acid (1 ml.) was heated under reflux for 40 hr., three further portions (20 ml.) of hydrochloric acid being added at 10-hr. intervals. The toluene layer was then separated and evaporated to a yellow semisolid residue (9·0 g.), the infrared spectrum of which showed absorption (5·8 and 5·9 μ) in the carbonyl region. This material (7 g.) was treated with diazomethane, and the product heated with 10% palladium–charcoal (1·4 g.) in a stream of carbon dioxide at 280° for 1·5 hr. and then at 330° (b. p.) for 4 hr. The organic material was distilled at 1 mm. from the catalyst, chromatographed in 2 : 1 light petroleum (b. p. 40—60°)–ether, and crystallised from methanol, to yield anthracene (0·2 g.), m. p. 215° (with sublimation) (Found: C, 94·6; H, 5·9%; *M*, 160·5. Calc. for $C_{14}H_{10}$: C, 94·4; H, 5·6%; *M*, 178). The m. p.s of the derived picrate (red needles, m. p. 145°) and the 1,3,5-trinitrobenzene complex (orange needles, m. p. 167—170°) were not depressed on admixture with authentic specimens.

Degradation of the Adduct (IIIc) *to Phenanthrene.*—A slurry of potassium borohydride (5 g.) in dry tetrahydrofuran (100 ml.) was added to a solution of the adduct (6·0 g.) in tetrahydrofuran and the mixture was stirred for 2 hr. Potassium borohydride (2 g.) and potassium

[14] Brunner, *Monatsh.*, 1913, **34**, 913.

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hydroxide (0·4 g.) in water (75 ml.) were added and stirring was continued overnight. The tetrahydrofuran layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with saturated brine and evaporated, to yield a yellow oil (5 g.) (mixture of triol esters). This material was heated with 10% palladium–charcoal (0·8 g.) in a slow stream of nitrogen at 210° for 1·5 hr. and then at 330—340° for 4 hr. The organic material (1 g.) that distilled at 300°/1 mm. from the catalyst was chromatographed in 2 : 1 light petroleum (b. p. 40—60°)–ether on alumina. The eluant, with picric acid, yielded phenanthrene picrate, m. p. 140—146° undepressed on admixture with an authentic specimen of m. p. 143—146°.

9-*Acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-12-*methoxycarbonyl*-3-*methyl*-1,4-*dioxophenanthrene* (IIIf).—The acetoxy-diene (I) (2·0 g.) was added to a solution of 6-methoxycarbonyltoluquinone [15] (IIf) (1·8 g.) in benzene (20 ml.); the solution became warm and was left overnight, and the solvent then removed under reduced pressure. Trituration of the residue with ether at 0° yielded 9-*acetoxy*-$\Delta^{2,9(14)}$-*decahydro*-12-*methoxycarbonyl*-3-*methyl*-1,4-*dioxophenanthrene* (IIIf) (2·2 g., 63%), m. p. 114—118°. A pure sample had m. p. to 116·5—118° and $\lambda_{max.}$ 243, 350—360 mμ (log ε 4·037, 1·978) (Found: C, 66·0; H, 6·6. $C_{19}H_{22}O_6$ requires C, 65·8; H, 6·4%).

9-*Acetoxy*-$\Delta^{9(14)}$-*dodecahydro*-12-*methoxycarbonyl*-3-*methyl*-1,4-*dioxophenanthrene*.—(*a*) A solution of 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-12-methoxycarbonyl-3-methyl-1,4-dioxophenanthrene (IIIf) (3 g.) in absolute methanol (150 ml.) was hydrogenated at 50 lb./sq. in. in the presence of Adams catalyst (0·5 g.). The catalyst was filtered off, and the filtrate concentrated to 10 ml.; it then deposited crystals of 9-*acetoxy*-$\Delta^{9(14)}$-*dodecahydro*-12-*methoxycarbonyl*-3-*methyl*-1,4-*dioxophenanthrene* (2·1 g., 70%), m. p. 143—147°. An analytical sample (from methanol) had m. p. 147—149° (Found: C, 65·7; H, 7·2. $C_{19}H_{24}O_6$ requires C, 65·5; H, 6·9%).

(*b*) Zinc powder (1 g.) was added to a stirred solution of the adduct (IIIf) (1 g.) in acetic acid (50 ml.). After 30 min. the insoluble material was filtered off and the residue obtained on removal of the acetic acid under reduced pressure was extracted with boiling light petroleum (b. p. 100—120°; 2 × 20 ml.). Evaporation of the extracts gave the crude dihydro-derivative (0·5 g.), m. p. 132—137°. Recrystallisation from methanol gave pure material, m. p. 145—148° identical with that prepared as in (*a*). The ultraviolet absorption spectrum of this compound showed no maximum in the range 200—350 mμ.

Degradation of the Adduct (IIIf).—The adduct (6·0 g.) was reduced with potassium borohydride, as described for the reduction of the adduct (IIIc), to a mixture of triol esters (6 g.) which was dehydrated 220—235° for 75 min. in a stream of nitrogen with powdered fused potassium hydrogen sulphate (9 g.). After addition of water the product was extracted with ether. The residue (3·8 g.) obtained on evaporation of the dried (K_2CO_3) extract was heated with selenium (10 g.) at 350° ±10° for 24 hr. The organic material was extracted with toluene, and the resulting solution boiled with sodium. After cooling and filtering, the solvent was removed and the residue chromatographed in light petroleum on alumina. Treatment of the eluted material (620 mg.) with picric acid yielded 3-methylphenanthrene picrate, m. p. 138—140°, from which was isolated 3-methylphenanthrene, m. p. 58—60° undepressed in admixture with an authentic sample [20] of m. p. 61·5—62·5°. Similar results were obtained when the dehydrogenation was carried out with palladium–charcoal

6-*Methoxy*-3-*methoxycarbonyltoluquinone* (IId).—4-Methoxycarbonyl-5-methylcyclohexane-1,3-dione [16] was treated with bromine (as described [17] for the ethyl ester), to yield *methyl* 3,5-*dibromo-orsellinate* (90%; m. p. 103—110°) which, when crystallised from dry methanol, had m. p. 107·5—109° (Found: C, 32·0; H, 2·3; Br, 46·3. $C_9H_8Br_2O_4$ requires C, 31·8; H, 2·4; Br, 47·0%). Stenhouse [18] obtained this compound by brominating methyl orsellinate but did not record its m. p. It was reduced, as for the ethyl ester,[17] except that palladium–charcoal and not palladium on polyvinyl alcohol was the catalyst. The resulting methyl orsellinate, m. p. 143—146° (lit.,[19] 140°), was methylated (to yield methyl everninate, 66%), and then oxidised (as described for the ethyl ester [6]) to methyl 4-methoxy-6-methylgentisate (34%), m. p. 154—156° (lit.,[6] 153—154°).

Silver oxide (15 g.) was added portion-wise to a shaken, boiling solution of methyl

[15] Nudenberg, Gaddis, and Butz, *J. Org. Chem.*, 1943, **8**, 500.
[16] Sonn, *Ber.*, 1929, **63**, 3014.
[17] Anker and Cook, *J.*, 1945, 311.
[18] Stenhouse, *Annalen*, 1863, **125**, 355.
[19] Herzig, Wenzel, and Kurzweil, *Monatsh.*, 1903, **24**, 898.

4-methoxy-6-methylgentisate (5 g.) in dry benzene (50 ml.) containing freshly dried potassium carbonate (5 g.), at such a rate that boiling was maintained. The solution was cooled to 50—60° for 15 min. and the insoluble material was filtered off and washed with hot dry benzene (30 ml.). Evaporation at <40° of the dried (K_2CO_3) combined filtrates gave the light yellow *6-methoxy-3-methoxycarbonyltoluquinone* (IId) (5 g., 100%), m. p. 76—82°, $\lambda_{max.}$ 267 mμ (log ε 4·12) (Found: C, 57·3; H, 5·1. $C_{10}H_{10}O_5$ requires C, 57·1; H, 4·8%). Recrystallisation from dry carbon disulphide did not improve the m. p. and sublimation caused decomposition.

Diels–Alder Reaction of 1-1′-*Acetoxyvinylcyclohexene* (I) *and* 6-*Methoxy-3-methoxycarbonyltoluquinone* (IId) (with B. W. Nash).—The quinone (3·0 g.), the diene (3·0 g.), and a crystal of quinol were heated at 100° under nitrogen for 60 hr. The resultant dark brown oil, when triturated with ether, yielded a solid which was filtered off and washed with ether, to yield an *adduct* (IIId or e) (2·1 g., 39%), m. p. 180—184°. An analytical sample (from dioxan or aqueous dioxan) had m. p. 181—183°, $\lambda_{max.}$ 278 mμ (log ε 3·81) (Found: C, 63·7; H, 6·6. $C_{20}H_{24}O_7$ requires C, 63·8; H, 6·4%). This material appeared to be polymorphic. When heated slowly the crystals became opaque at 75—95° but melting did not occur until 180°. When heated rapidly from room temperature it melted at ~120°, and when immersed in a bath at 160° it melted instantly.

Methanolysis of the Adduct (IIId) *or* (IIIe).—A solution of the adduct (20 g.) in dry methanol (600 ml.) containing " AnalaR " sulphuric acid (7 ml.) was heated under reflux for 30 min., then concentrated to 100 ml. under reduced pressure and cooled. The crystalline product (13·2 g., 74%), when washed with methanol and dried, had m. p. 160—180°. The pure Δ^2-*dodecahydro*-2(or 3)-*methoxy*-12(or 11)-*methoxycarbonyl*-11(or 12)-*methyl*-1,4,9-*trioxophenanthrene* (recrystallised from methanol) had m. p. 200—202° (Found: C, 64·7; H, 6·6; MeO, 18·6. $C_{18}H_{22}O_6$ requires C, 64·8; H, 6·4; MeO, 18·9%).

Dimethyl 2,5-*Dihydroxyterephthalate*.—A cold (0°) solution of bromine (4·26 ml.) in chloroform (100 ml.) was added to dimethyl 2,5-dioxocyclohexane-1,4-dicarboxylate [20] (9·4 g.) in chloroform (100 ml.) also at 0°. The solution was kept at room temperature for 2 hr., then at 40° for 2 hr., washed with 10% sodium thiosulphate solution, then with water, and dried (K_2CO_3). Evaporation at reduced pressure left *dimethyl* 2,5-*dihydroxyterephthalate* (8 g., 85%), m. p. 170—175°. The pure compound (a yellow fluorescent solid from benzene) had m. p. 177—179° (Found: C, 53·2; H, 4·4. $C_{10}H_{20}O_6$ requires C, 53·1; H, 4·4%), $\lambda_{max.}$ 3·1w (OH) and 5·98s μ (C=O). Its diacetate had m. p. 168·5—171° (lit.,[9] 166—168°).

Dimethyl 2,5-*Dihydroxy*-3,6-*dinitroterephthalate*.—An excess of a solution of oxides of nitrogen [10] in carbon tetrachloride was added to a stirred suspension of dimethyl 2,5-dihydroxyterephthalate (1·0 g.) in the same solvent. Stirring was continued for 30 min. and then the light yellow product was filtered off, washed with a little carbon tetrachloride, and dried, to yield the *dinitro-ester* (0·7 g.), m. p. 153° (decomp.). The pure compound formed light yellow plates (from benzene or methanol), m. p. 245° (decomp.) (Found: C, 38·4; H, 2·4; N, 8·7. $C_{10}H_8N_2O_{10}$ requires C, 38·0; H, 2·5; N, 8·9%), $\lambda_{max.}$ 3·22 (OH) 5·95 (ester C=O), and 6·45 and 7·50 μ (NO_2). The derived *diacetate*, recrystallised from methanol, had m. p. 183·5—186·5° (Found: C, 42·0; H, 3·1. $C_{14}H_{12}N_2O_{12}$ requires C, 42·0; H, 3·0%). Oxidation in the presence of potassium carbonate with dried oxides of nitrogen gave a nitrogenous product.

Quinhydrone of 2,6-*Dimethoxycarbonylbenzoquinone*.—To a stirred solution of dimethyl 2,5-dihydroxyterephthalate (13 g.) in dry benzene (750 ml.) containing anhydrous magnesium sulphate (26 g.) at 55° silver oxide (39 g.) was added. The temperature was kept at 55° for 3 hr., and the insoluble material then filtered off and washed with dry benzene. Evaporation of the combined filtrates yielded a mixture (10 g.) of a red and a yellow solid. This mixture was extracted with boiling ether (4 × 100 ml.), and the extracts were cooled to 0° for 16 hr.; mainly dimethyl 2,5-dihydroxyterephthalate (1·2 g.) was deposited. Evaporation of the extracts gave mainly red crystals (1·9 g.; m. p. 120—170°) which when purified by fractional crystallisation from ether and benzene or by sublimation gave the essentially pure, red *quinhydrone*, m. p. 140—142° (Found: C, 53·4; H, 4·2. $C_{20}H_{18}O_{12}$ requires C, 53·4; H, 4·0%), $\lambda_{max.}$ 3·0vw (OH), 5·79s, and 6·01s μ (C=O). The quinone content of this material was estimated [13] as 45%.

Diels–Alder Reaction of 2,5-*Dimethoxycarbonylbenzoquinone*.—(*a*) Dimethyl 2,5-dihydroxyterephthalate (1 g.) was dissolved in dry benzene (50 ml.) together with 1-1′-acetoxyvinylcyclohexene (1 g.). Freshly dried magnesium sulphate (2 g.) and silver oxide (3 g.) were added

[20] Prepared by method described by Hauser and Boyd, *Org. Reactions*, 1942, **1**, p. 283, for ethyl ester.

and the mixture was stirred at 45—50° for 3 hr. The resultant mixture was filtered and the filtrate evaporated, to yield a yellow solid from which the excess of diene was extracted with boiling light petroleum (b. p. 100—120°; 25 ml.). The resultant solid crystallised from methanol and acetic acid, to yield the *bis-adduct* as white needles (0·15 g.), m. p. 228—230°. This material resolidified to cubes which melted at 274—276° (Found: C, 65·2; H, 6·4%; *M*, 390. $C_{30}H_{36}O_{10}$ requires C, 64·8; H, 6·5%; *M*, 556).

(*b*) A solution of the quinhydrone of 2,5-dimethoxycarbonylbenzoquinone (1·9 g.) in dry benzene (25 ml.) was stirred at 55° while 1-1′-acetoxyvinylcyclohexene (1·3 g.) in benzene (50 ml.) was added dropwise during 2 hr. After a further 2 hr. at 55° the solvent was removed and the residue extracted with boiling light petroleum (b. p. 100—120°; 25 ml.) [to remove dimethyl 2,5-dihydroxyterephthalate (0·3 g.)]. The residue (1·2 g.) recrystallised from methanol and acetic acid to yield the above bis-adduct, m. p. 228—230°.

We are indebted to Dr. J. W. Lown for the determination and interpretation of the nuclear magnetic resonance spectra which were measured on deuterochloroform solutions with a Varian Associates high-resolution spectrometer (model V-4311) at a fixed oscillator frequency of 56·45 Mc. Line positions were measured by the conventional side-band technique with a Muirhead–Wigan Decade oscillator (model D-695A) from tetramethylsilane as an internal reference. We also thank Dr. R. F. Garwood for helpful discussions, the University of London Central Research Fund for financial assistance, and the D.S.I.R. for an award (to G. C. C.). The infrared spectra were determined by Mr. P. Cook of this department.

Queen Mary College (University of London),
Mile End Road, London, E.1. [*Received, October 25th,* 1960.]

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559. *Polysaccharides of the Characeae. Part I. Preliminary Examination of a Starch-type Polysaccharide from* Nitella translucens.

By D. M. W. Anderson and N. J. King.

The fresh-water green alga, *Nitella translucens*, gives an iodophilic glucan in 4% yield (dry-weight basis). This material, which is very difficult to extract and purify satisfactorily, has been examined by chemical, enzymic, and physical methods.

Extraction by chloral hydrate yields a severely degraded product which has an abnormal potentiometric iodine-titration curve. Extraction by perchloric acid gives a more satisfactory product having a limiting viscosity number of 40; the amylose content is 12%, and the amylopectin component, which has an average chain length of 19 glucose units, appears to be similar in structural properties to plant amylopectins.

The fresh-water green alga, *Nitella translucens* (class, Chlorophyceae; order, Charales; family, Characeae) is of current interest since its long, filamentous, internodal cells (up to 40 cm. long) facilitate certain biophysical and physiological experiments.[1,2] Little is known of the chemical constitution of the Characeae; at the request of the Biophysics Department of this University, the polysaccharide components of both *Nitella translucens* and *Chara australis* have been studied. This paper reports a preliminary study of the iodophilic glucan isolated from *Nitella translucens*.

Both salt-water and fresh-water green algae are included in the Chlorophyceae, and authorities[3] consider species of protozoa, such as *Polytoma*, *Polytomella*, and *Prototheca*, to be colourless members of the Chlorophyceae. Although much is known of the metabolism of algae,[3] few studies of the carbohydrate systems in such materials have been

[1] Mercer, Hodge, Hope, and Maclean, *Austral. J. Biol. Sci.*, 1955, **8**, 1.
[2] Walker, *Austral. J. Biol. Sci.*, 1955, **8**, 476.
[3] Fogg, "The Metabolism of Algae," Methuen, London, 1953.

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reported.[4,5] Investigations of algal cell components[5,6] must be distinguished from studies of the soluble extracellular materials exuded by some algae.[7]

According to Fogg,[3] the Chlorophyceae tend to be ancestral to land flora, having starch and fat as reserve materials; the starch is considered to be essentially similar to that from land plants (Fogg, p. 93). Although it is clear that the " paramylon granules "[8] reported in early studies may be starch-like (*e.g.*, for *Polytoma uvella*[9] and *Polytoma obtusum*[10]), recent work has shown that the " paramylon " from *Ochromonas malhamensis*[11] and from *Euglena* species[12] (which do not belong to the Chlorophyceae) resemble laminarin. Recent chemical investigations on *Polytomella coeca*[13] and *Dunaliella bioculata*[5] however support Fogg's statements, but it must not be presumed that the polysaccharide systems of all members of the Chlorophyceae will be similar to those of land plants. Indeed, *Cladophora rupestris*[6,14] is reported to contain laminarin rather than starch. This is of interest since Cronshaw *et al.*[15] found, by *X*-ray and electron-microscopical studies, that *Cladophora rupestris* and *Chaetomorpha melagonium*, from four green marine algae examined, had cell-wall structures resembling those of land plants: it was also observed that chemically differing carbohydrates can give the same *X*-ray diffractogram.[15] Recent *X*-ray evidence[16,17] has suggested the presence of differing " degrees of order " in tuber and algal starches, including an unidentified species of *Nitella*.

An early study[18] of an unnamed species of *Nitella* showed a cellulose-type polyglucan to be present; tests for starch were negative. However, iodophilic starch-like granules, enclosed within a membrane, were later observed[1] in *Nitella* species.

Experimental and Results

Analytical Methods.—Conventional carbohydrate techniques were used throughout.

Collection of Material.—*Nitella translucens* (authenticated by Dr. A. J. Brook) was collected on May 19th, 1959, from Loch Cardney, Dunkeld, Perthshire. The filamentous algal cells were easily snapped, with resultant loss of the cell inclusions, and were therefore handled as carefully as possible during collection. The cells were individually freed by hand from traces of debris and other pond-weeds. The raw material contained: N 2·3, 2·1%; ash 14·1, 13·7%; uronic anhydride 24·1, 24·4%. A methoxyl content of $<0·2\%$ may arise from the chlorophyll present.

Preparation of Crude Starch.—The cells were homogenised in water chilled to 0° by brief treatments in an " Atomix " homogeniser. The turbid fluid was poured through a double layer of muslin. The combined residues were re-homogenised with chilled water; this extraction process was carried out 4 times in all.

The dark-green sediment was exhaustively defatted (Soxhlet), giving material which was stained blue-black with iodine solution (yield, 21%, dry-weight basis) (Found: N, 4·6; uronic anhydride, 13·0; ash, 24·4; SO_4'', 0·8%). Paper chromatography of a hydrolysate showed that galactose, glucose, arabinose + mannose, and xylose were present in the ratio 1·5 : 92 : 5·5 : 1; cuprimetric determinations[19] of the total reducing power after hydrolysis indicated 21% of free sugar (as glucose). Calculation therefore shows that the total amount of starch present was $>4\%$ (dry weight basis).

[4] Hirst, *Proc. Chem. Soc.*, 1958, 177.
[5] Eddy, Fleming, and Manners, *J.*, 1958, 2827.
[6] Fisher and Percival, *J.*, 1957, 2666.
[7] Lewin, *Canad. J. Microbiol.*, 1956, **2**, 665.
[8] Gottleib, *Ann. Chem. Pharm.*, 1850, **75**, 50.
[9] Pringsheim, *Naturwiss.*, 1935, **23**, 120.
[10] Brechot, *Compt. rend. Soc. Biol.*, 1937, **126**, 555.
[11] Archibald and Manners, *Chem. and Ind.*, 1958, 1516.
[12] Clark and Stone, *Biochim. Biophys. Acta*, 1960, **44**, 161.
[13] Bourne, Stacey, and Wilkinson, *J.*, 1950, 2694.
[14] Kylin, *Kgl. Fysiograf. Süllskap. Lund Forh.*, 1944, **14**, 221.
[15] Cronshaw, Myers, and Preston, *Biochim. Biophys. Acta*, 1958, **27**, 89.
[16] Meeuse and Kreger, *Biochim. Biophys. Acta*, 1954, **13**, 593.
[17] Meeuse and Kreger, *Biochim. Biophys. Acta*, 1959, **35**, 26.
[18] Hough, Jones, and Wadman, *J.*, 1952, 3393.
[19] Somogyi, *J. Biol. Chem.*, 1952, **195**, 19.

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Attempted Deproteinisation.—The action of (*a*) proteolytic enzymes, (*b*) trichloroacetic acid, and (*c*) a modified Sevag denaturation process, previously found effective in freeing cereal starches from protein,[20] failed to reduce the nitrogen content significantly. Since other protein precipitants had been ineffective on material of somewhat similar origin,[6] methods of extracting the glucan preferentially from the inorganic and proteinaceous material were applied.

(1) *Alkali-swelling and leaching with hot water.* These gave a cream-coloured powder (Found: N, 1·8%). An aqueous solution was stained blue with iodine ($\lambda_{max.}$ 585 mμ). Hydrolysis gave glucose with very small amounts of xylose and arabinose; cuprimetric titration showed that the glucan was 76% pure. On α-amylolysis,[21] conversion into maltose (P_M) = 60% in 6 hr., 76% in 24 hr., and addition of iodine–potassium iodide solution then gave no reaction. On β-amylolysis, P_M = 54 (24 hr.), 59 (48 hr.). 1·15 mol. of periodate were reduced [22] per anhydroglucose unit after 190 hr.

(2) *Extraction by chloral hydrate.* Exhaustive extraction [23] with 33% aqueous chloral hydrate at 70° under nitrogen gave a pale cream-coloured product (26%). A solution in hot water did not reduce Fehling's solution, had $[\alpha]_D^{16}$ +163° (*c* 1·0% in water), and gave a blue colour with iodine solution (Found: N, 0·8%). Hydrolysis and paper chromatography gave only glucose and xylose (98 : 2). Cuprimetric determinations,[19] with correction for the trace of xylose present, gave the purity of the glucan as 91, 90, 92, 92% (control determinations on purified oat starch [20] gave 96, 99, 97, 96%). On α-amylolysis, P_M = 70% (4 hr.), 82% (24 hr.), 83% (48 hr.). On β-amylolysis at pH 4·6, P_M = 56% (24 hr.), 62% (48 hr.). Viscosity measurements were made [24] in 0·1M-potassium chloride solution in a modified Ubbelohde viscometer. Extrapolation to zero concentration of the usual viscosity graph gives $[\eta]$ = 24·4.

The glucan (51·2 mg.) was oxidised at 0° with sodium metaperiodate [25] in a total volume of 50 ml. with the following results:

Time of oxidation (days)	1	3	6	9	11
Periodate (mol.) reduced per anhydroglucose unit (ref. 26)	0·91	0·95	0·99	1·01	1·03
0·00714N-Formic acid (ml.) released per 5 ml. (ref. 27)	0·25	0·29	0·30	0·30	0·31

Hence the average chain length = 15 anhydro-glucose units, if no amylose was present.

The " blue-value " [28] (B.V.) of the glucan and of ten starches (whose amylose content had earlier been found by the potentiometric method [29]) was determined. The values found are shown in Table 1.

TABLE 1.

Source of starch *	Amylose (%) *	Blue value	Source of starch *	Amylose (%) *	Blue value
Oat	26·0	0·365	Pearl manioc	15·7	0·241
Barley	22·0	0·370	Parsnip	11·1	0·159
Potato I	20·4	0·372	Oat amylopectin	3·2	0·071
Sweet potato	17·8	0·287	Waxy maize	1·4	0·044
Banana	16·8	0·294	*Nitella translucens*	?	0·161
Tapioca	16·7	0·270			

* Origin of samples and amylose contents as quoted in ref. 29.

The graph of B.V. against amylose content (see Fig. 1) indicated that the *Nitella* starch contained 10—11% of amylose. Although there is no simple general relation between blue value and amylose content, an approximately linear relation apparently holds for amylose contents of <18%.

Potentiometric iodine titrations [29] of the glucan gave curve A in Fig. 2, from which it was not possible to obtain the amylose content by extrapolation. The glucan gave no reaction with " concanavalin A " (result by courtesy of Dr. D. J. Manners and Dr. A. Wright).

(3) *Exhaustive extraction with* 30% *aqueous perchloric acid.* Such extraction at room

[20] Anderson and Greenwood, *J. Sci. Food Agric.*, 1955, **6**, 587.
[21] Liddle and Manners, *J.*, 1957, 3432.
[22] Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1216.
[23] Meyer, Brentano, and Bernfeld, *Helv. Chim. Acta*, 1940, **23**, 845.
[24] I.U.P.A.C., *J. Polymer Sci.*, 1952, **8**, 257.
[25] Potter and Hassid, *J. Amer. Chem. Soc.*, 1948, **70**, 3488.
[26] Halsall, Hirst, and Jones, *J.*, 1947, 1399.
[27] Anderson, Greenwood, and Hirst, *J.*, 1955, 225.
[28] Bourne, Haworth, Macey, and Peat, *J.*, 1948, 924.
[29] Anderson and Greenwood, *J.*, 1955, 3016.

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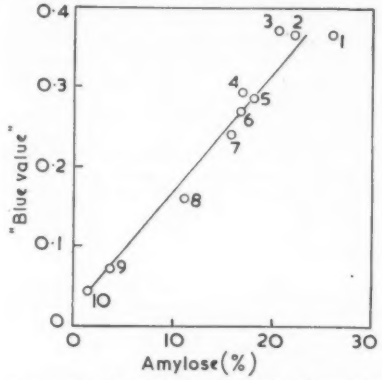
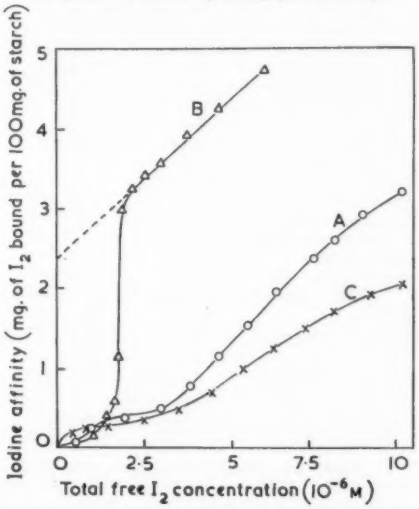
temperature [30] gave a product which was precipitated and purified as iodine complex. The final product was freeze-dried (yield, 5%); it had $\lambda_{max.}$ 585 mμ, $[\alpha]_D^{16}$ +170° (*c* 1% in water) (Found: N = 0·8%). After hydrolysis, glucose + xylose (98 : 2) were detected by paper chromatography; cuprimetric determination [19] showed that the glucan was 90% pure. On α-amylolysis, P_M = 53% (3 hr.), 77% (24 hr.); β-amylolysis at pH 4·6 gave P_M = 50% (24 hr.), 61% (48 hr.). From viscosity measurements, extrapolation of the graph gave $[\eta]$ = 40. Viscosity determinations on parsnip starch [31] and on a commercial sample of waxy maize starch gave $[\eta]$ = 44 and 40 respectively.

FIG. 1. *Plot of amylose content (potentiometric titration) against "blue value" for materials of low amylose content.*



1, oat starch; 2, barley starch; 3, potato starch; 4, banana starch; 5, sweet potato starch; 6, tapioca; 7, pearl manioc starch; 8, parsnip starch; 9, oat amylopectin; 10, waxy maize starch: origins as quoted in ref. 29.

FIG. 2. *Potentiometric iodine-titration curves (standard conditions as in ref. 29) for*: A, *N. translucens* glucan (chloral hydrate), B, *N. translucens* glucan (perchloric acid), C, Protozoal glucan (chloral hydrate) (see ref. 36).



The glucan (101·2 mg.) was oxidised [27] at room temperature with potassium metaperiodate (final vol. 50 ml.) with the following results:

Time of oxidation (days)	3	6	9	11
Periodate (mol.) reduced per anhydroglucose unit (ref. 26)	0·60	0·76	0·95	0·97
0·00714N-Formic acid (ml.) released per 5 ml. (ref. 27)	0·28	0·38	0·42	0·43

Hence the average chain length is 21 units, and that of the amylopectin component (if the glucan contains 12% of amylose) is 19 glucose units. The product resulting from periodate oxidation for 11 days was isolated, dialysed, and hydrolysed. Paper chromatography revealed a small amount of xylose but no glucose.

Potentiometric iodine titration [29] of the glucan (20·02 mg.) gave curve B in Fig. 2. This curve is of similar shape to that given by plant starches and indicates the presence of 12% of amylose.

Discussion

The crude material extracted as a cold-water sediment was very difficult to purify. Initial attempts to deproteinise the starch consumed considerable amounts of material without success (cf. ref. 6). Extraction with cold alkali and hot water gave, in poor yield, a glucan of 76% purity, a result similar to that (69%) reported [5] for *D. bioculata*.

Chloral hydrate gave a relatively pure glucan (90%; cf. ref. 32) which was severely degraded (periodate oxidation and viscosity results) and gave an abnormal potentiometric iodine titration curve (see below).

[30] Pucher, Leavenworth, and Vickery, *Analyt. Chem.*, 1948, **20**, 850.
[31] Anderson and Greenwood, *J.*, 1956, 220.
[32] Archibald, Hirst, Manners, and Ryley, *J.*, 1960, 556.

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Although the yield was poor, the glucan extracted by perchloric acid was, comparatively, much less degraded. Indeed, its limiting viscosity number and amylose content were similar to that of parsnip starch which is therefore included in Table 2, together with the present results and the values reported for commercial waxy maize starch, a salt-water alga,[5] and a green seaweed.[33] The properties of algal starches can now be compared [32,33,34] with those of glycogens and floridean, plant, and protozoal starches, though only a preliminary investigation of our glucan could be made with the material available.

TABLE 2.

Source of glucan	*N. translucens* * (fresh-water alga)		*D. bioculata* [5] (salt-water alga)	*C. filiformis* [33] (green seaweed)	Parsnip starch [31]	Waxy maize starch ¶
Method of extraction	perchloric acid	chloral hydrate	perchloric acid	see ref. 33	cold water	commercial sample
$[\alpha]_D$ (c 1% in H_2O)	+170°	+163°	+169°	+154°	+166°	+170°
$\lambda_{max.}$ of I_2 complex (mμ)	585	590	600	540	590	555
Blue value	0·16	0·16	—	—	0·16	0·04
Amylose (%) (I_2 titrn.)	12	?	12—14	0	11 [29]	1 [29]
β-Amylolysis limit	61	62	62	57	72 ‡	54 [34]
α-Amylolysis limit	77	82	85	90	85	88 †
IO_4^- reduction (mole per anhydroglucose unit)	0·97	1·03	—	0·95	1·03 ‖	1·05 [27]
Av. chain length ($\overline{C.L.}$)	21	15	18	21	23 [27]	20 [27]
Hence amylopectin $\overline{C.L.}$	19	13	15—16	21	20·4 [27]	20 [27]
Limiting viscosity no. [η]	40	24	—	15	44	40
Av. internal C.L.§	5—6	3—4	3—4	6—7	6—7	6—7 [34]
Av. external C.L.§	13—14	9—10	12	14—15	13—14	14—15 [34]

* Analytical values are based on the determined glucose content (cf. ref. 32). † Data from *J.*, 1956, 2831. ‡ Data from *Stärke*, 1960, **12**, 169. § As calculated in ref. 21. ‖ D. M. W. Anderson, Ph.D. Thesis, Edinburgh, 1956. ¶ Same sample as used in refs. 27 and 29. A different sample, having $[\alpha]_D$ 212°, [η] 150, is presumably referred to in refs. 33 and 34.

The differences between the products obtained by use of chloral hydrate and perchloric acid suggest that the amylose-type component in algal starches may be highly labile and very easily degraded. Although chloral hydrate was stated [13] to be the best extractant for similar materials, it was later found [5] to cause more extensive degradation (cf. ref. 32) than perchloric acid.

Abnormal iodine-titration curves, similar in shape to that given by the chloral hydrate product, have been noted previously [35] for proteinaceous, floridean, and protozoal starches, for degraded samples, and for certain amylopectins obtained by fractionation; degradation, contamination with protein or waxy materials (cf. ref. 29) and possibly also the presence of abnormal linkages can all distort the normal shape of the titration curve. A value for the amylose content, in good agreement with that found by iodine titration for the perchloric acid product, was, however, deduced from the "blue-value" of the chloral hydrate material. This suggests that the degradation, although severe, had not proceeded below the achroic limit. Since both glucans had very similar nitrogen contents, it is possible that in this instance the abnormal curve resulted primarily from the degradation caused during extraction. The iodine-titration curve (Fig. 2, curve C) given by a

[33] Mackie and Percival, *J.*, 1960, 2381.
[34] Manners and Ryley, *Biochem. J.*, 1955, **59**, 369.
[35] Anderson and Greenwood, unpublished results.

protozoal starch [36] is strikingly similar in shape; since the amylose content was stated—on the basis of a low B.V.—to be negligible,[36] re-examination of protozoal starches extracted [37] with chloral hydrate may now be desirable. It is unusual for no amylose to be detectable in amylopectin-type glucans, *e.g.*, in the " waxy " starches or in fractionation products.

On this basis, the results quoted for an amylopectin-type glucan [33] may also bear re-investigation since the mode of extraction involved addition of a quaternary ammonium salt. Amylose is precipitated by such reagents,[38] and some fractionation may inadvertently have been effected.

We thank Professor E. L. Hirst, C.B.E., F.R.S., for his interest, and the Department of Scientific and Industrial Research for a maintenance grant (to N. J. K.). We are grateful to Dr. J. Dainty, Department of Biophysics, University of Edinburgh, for suggesting the study, and thank members of his staff and Dr. A. J. Brook, Department of Botany, for their assistance is locating and collecting supplies of the alga. We thank Dr. D. J. Manners for the supply of α- and β-amylase.

Department of Chemistry, University of Edinburgh. [*Received, December 12th*, 1960.]

[36] Forsyth and Hirst, *J.*, 1953, 2132.
[37] Forsyth, Hirst, and Oxford, *J.*, 1953, 2030.
[38] Fishman and Miller, *J. Colloid Sci.*, 1960, **15**, 232.

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560. *A Convenient Alternative Synthesis of 5-Hydroxytryptamine.**

By L. Bretherick, K. Gaimster, and W. R. Wragg.

A novel 7-stage synthesis of 5-hydroxytryptamine (I) from readily accessible starting materials, suitable for comparatively large-scale working, is described. *p*-Benzyloxybenzenediazonium chloride is condensed with ethyl α-acetyl-δ-phthalimidovalerate and the product is cyclised to ethyl 5-benzyloxy-3-2′-phthalimidoethylindole-2-carboxylate (II; R = O·CH_2Ph, R′ = CO_2Et). Relatively standard reactions lead from this ester to 5-hydroxytryptamine, which is isolated as its creatinine sulphate complex in 18·5% overall yield.

Several syntheses of 5-hydroxytryptamine (I) have been described.[1] In most of these the aminoethyl side chain is built up stepwise from a 5-hydroxyindole in which the hydroxy-group is protected and the 3-position unsubstituted. In such syntheses, particularly those of Hamlin and Fischer [1a] and Ash and Wragg,[1b] yields at the terminal stages are variable, so we sought a synthesis in which the side chain in a protected form was introduced at an early stage, and for which the starting materials required were readily available.

Apart from Harley-Mason and Jackson's synthesis,[1c] which is described on a scale giving only 0·63 g. of product, earlier syntheses [1d] along this line have involved relatively inaccessible intermediates or given poor yields. By adapting a synthesis [2] of ethyl 3-2′-phthalimidoethylindole-2-carboxylate (II; R = H, R′ = CO_2Et), we have obtained the 5-benzyloxy-analogue (II; R = O·CH_2Ph, R′ = CO_2Et) which proved a convenient intermediate, and could be made from readily accessible starting materials.

* Part of this work is the subject of B.P. Appl. 33,140/55.

[1] (*a*) Hamlin and Fischer, *J. Amer. Chem. Soc.*, 1951, **73**, 5007; (*b*) Ash and Wragg, *J.*, 1958, 3887, and the references cited therein; (*c*) Harley-Mason and Jackson, *J.*, 1954, 1165; (*d*) Bernini, *Ann. Chim.* (*Italy*), 1953, **43**, 559; Vejdelek and Tuma, *Cesk. Farm.*, 1955, **4**, 510; Abramovitch and Shapiro, *J.*, 1956, 4589; Sucros, Span.P., 227,606; *Chem. Abs.*, 1958, **52**, 2923; (*e*) Young, *J.*, 1958, 3493; Pietra. *Il Farmaco*, Ed. Sc., 1958, **13**, 75; Nenitzescu and Raileanu, *Chem. Ber.*, 1958, **91**, 1141.
[2] Keimatsu, Sugasawa, and Kasuya, *J. Pharm. Soc. Japan*, 1928, **48**, 762.

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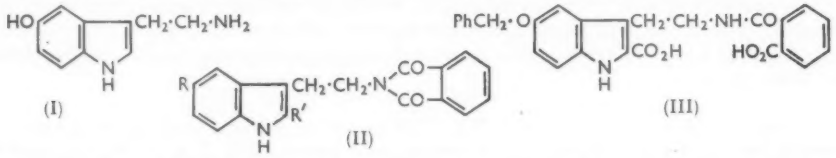
Ethyl α-acetyl-δ-phthalimidovalerate, obtained [2] in 96% yield from 3-phthalimidopropyl bromide and ethyl acetoacetate, coupled smoothly with *p*-benzyloxybenzenediazonium chloride [1b] in the presence of sodium acetate, and the resulting crude phenylhydrazone (>90% yield) was cyclised by saturating its boiling ethanolic solution with



hydrogen chloride (Method A) to give ethyl 5-benzyloxy-3-2′-phthalimidoethylindole-2-carboxylate (II; R = O·CH_2Ph, R′ = CO_2Et) in 51—58% overall yield on 0·75-mole scale. Alkaline hydrolysis of this ester gave a 98% yield of the diacid (III) which at 240—250° reproducibly underwent concomitant decarboxylation and dehydration to give 5-benzyloxy-3-2′-phthalimidoethylindole (II; R = O·CH_2Ph, R′ = H) in 84% yield on a 100-g. scale. Contrary to experience in an analogous preparation of 5-benzyloxyindole,[1b] the use of copper chromite in boiling quinoline for this decarboxylation was disadvantageous.

5-Benzyloxy-3-2′-phthalimidoethylindole was converted smoothly into 5-benzyloxytryptamine (isolated as the neutral sulphate) in 68—73% yield by an excess of hydrazine hydrate in boiling ethanol. Reductive debenzylation of the sulphate in the presence of palladium–charcoal gave crude 5-hydroxytryptamine, isolated as its monohydrated complex (m. p. 217—219°) with creatinine sulphate [3] in over 90% yield. Recrystallisation from aqueous ethanol gave analytically pure material, m. p. 219—221° (decomp.), with the correct ultraviolet spectrum.[4]

Experimental

M. p.s determined in evacuated capillaries are designated m. p. (e.c.).

Ethyl 5-Benzyloxy-3-2′-phthalimidoethylindole-2-carboxylate.—Method A. *p*-Benzyloxyaniline (150 g., 0·75 mole), dissolved in boiling ethanol (300 ml.), was treated as rapidly as possible with a mixture of concentrated hydrochloric acid (300 ml.) and water (450 ml.) followed by ice (600 g.). To this stirred suspension was added sodium nitrite (68 g., 0·975 mole) in water (150 ml.) during about 20 min. and the suspension was stirred for a further 40 min. at 5—10° (cooling). The solution was then treated with charcoal and filtered.

Ethyl α-acetyl-δ-phthalimidovalerate (237 g., 0·75 mole) was dissolved in warm ethanol (1100 ml.), and to the cooled solution was added anhydrous sodium acetate (615 g.) and ice (500 g.). To this stirred mixture at 5° was added rapidly the filtered solution of diazotised *p*-benzyloxyaniline described above, and the whole was stirred while being allowed to attain room temperature. The red viscous oil which separated was extracted with benzene (3 × 450 ml.), and the extracts were dried (Na_2SO_4) and evaporated. A solution of the crude phenylhydrazone in dry ethanol (1600 ml.) was saturated at the b. p. with a rapid stream of hydrogen chloride, then cooled in ice. The solid was filtered off, washed with ice-cold ethanol (2 × 400 ml.) and with water (2 × 400 ml.), and dried at 80°, to give the required *ester* (178 g., 51%) as needles, m. p. 188—190° (Found: C, 72·0; H, 5·15; N, 6·0. $C_{28}H_{24}N_2O_5$ requires C, 71·9; H, 5·1; N, 6·0%).

Method B. To secure reproducible results on increasing the scale of this preparation to 5 moles, we used the technique [1b] found optimum for the preparation of the corresponding 3-unsubstituted 5-benzyloxyindole-2-carboxylic ester. This involved addition of ethanol (3 vol.), saturated with hydrogen chloride at 0°, to a cold ethanolic solution (1 vol.) of the crude hydrazone; an exothermic reaction then occurred. While this method gave a similar yield (54—58%) to method A, the ester prepared *via* method B had m. p. 186—188°; its infrared and ultraviolet spectra were nevertheless identical with those of the material (m. p. 188—190°) prepared by method A. However, the diacid (III) obtained by hydrolysis of the lower-melting ester gave a low yield (45—48%) of poor quality product on dehydration and decarboxylation

[3] Speeter, Heinzelmann, and Weisblat, *J. Amer. Chem. Soc.*, 1951, **73**, 5514.
[4] Rapport, *J. Biol. Chem.*, 1949, **180**, 961.

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by the one-step procedure described below; this diacid could nevertheless be used satisfactorily by carrying out the dehydration [5] and decarboxylation separately as described in the two-step procedure below, provided that the decarboxylation was restricted to 20-g. batches.

5-Benzyloxy-3-(2-o-carboxybenzamidoethyl)indole-2-carboxylic Acid (III).—Ethyl 5-benzyloxy-3-2′-phthalimidoethylindole-2-carboxylate (135 g., 0·288 mole) was suspended in ethanol (500 ml.). Potassium hydroxide (158 g., 2·8 moles) in water (1·8 l.) was added, and the mixture was warmed on the steam-bath until dissolution was complete (15 min.) and then refluxed for 1·5 hr. Most of the ethanol was then distilled off. The residue was cooled at 10°, acidified with 4N-hydrochloric acid, and set aside. The solid which separated was filtered off and washed with water, to give the almost colourless acid (129 g., 98%), m. p. 230—235° (decomp.) after dehydration at about 200°. Satisfactory analytical figures could not be obtained for this compound.

5-Benzyloxy-3-2′-phthalimidoethylindole.—(a) *One-step procedure.* 5-Benzyloxy-3-(2-*o*-carboxybenzamidoethyl)indole-2-carboxylic acid (100 g., 0·218 mole) was melted and then stirred at 250°, the evolved carbon dioxide being removed by a stream of nitrogen. Decarboxylation was complete in about 1·5 hr. The residue, which on cooling solidified to a glass, was dissolved in hot ethyl methyl ketone (about 1 l.) and a small quantity of insoluble material was removed. The filtrate was concentrated to about 300 ml. and hot ethanol (900 ml.) was added. The solid which crystallised on cooling was filtered off and washed with cold ethanol (100 ml.). A second crop was obtained by concentration. The two crops were combined and suspended in cold N-sodium hydroxide; the solid was filtered off and washed with water and then with cold ethanol. The *phthalimido-compound* (73 g., 84%) was obtained as pale yellow prisms, m. p. 179—181° (Found: C, 75·9; H, 5·16; N, 7·0. $C_{25}H_{20}N_2O_3$ requires C, 75·8; H, 5·05; N, 7·05%).

(b) *Two-step procedure.* 5-Benzyloxy-3-(2-*o*-carboxybenzamidoethyl)indole-2-carboxylic acid (626 g.) was refluxed with acetic acid (6·5 l.) for 5 hr. and the hot mixture filtered from a little undissolved material. The product was filtered off at 20° and recrystallised from acetic acid (5·5 l.). The product was washed by resuspension in cold water (2 × 4 l.) and dried *in vacuo*, giving *5-benzyloxy-3-2′-phthalimidoethylindole-2-carboxylic acid* (423 g., 71%), m. p. 250—251° (decomp.) (Found: C, 70·8; H, 4·8; N, 6·4. $C_{26}H_{20}N_2O_5$ requires C, 70·9; H, 4·5; N, 6·4%).

5-Benzyloxy-3-2′-phthalimidoethylindole-2-carboxylic acid (20 g.) was decarboxylated at 260—270° under nitrogen during 45 min. The cold residual glass was dissolved in boiling ethyl methyl ketone (154 ml.), and the hot solution filtered, concentrated to *ca.* 60 ml., and treated with hot ethanol (192 ml.). The solid which separated was then treated as previously described, to give 17 g. (70%) of product, m. p. 181—182°.

5-Benzyloxytryptamine Sulphate.—5-Benzyloxy-3-2′-phthalimidoethylindole (32·5 g., 0·082 mole), 80% hydrazine hydrate (15·5 ml., 0·246 mole), and ethanol (850 ml.) were refluxed together for 2·5 hr. The solution was evaporated on a steam-bath, at reduced pressure in the final stages. 2N-Sodium hydroxide (250 ml.) was added to the warm residue, followed by ether (400 ml.), and the whole was cooled in ice until solid separated. After removal of this solid by filtration through "Hyflo," the ethereal layer was separated and washed with water until free from alkali. The base was extracted into N-acetic acid (150 ml.) and treated dropwise with an excess of concentrated sulphuric acid. The crude sulphate was washed with ice-water until free from acid and recrystallised (charcoal) from water. 5-Benzyloxytryptamine sulphate monohydrate (20 g., 73%) was obtained as almost colourless plates, m. p. (e.c.) 187—189° (Found: C, 61·3; H, 6·5; N, 8·3; S, 4·95. Calc. for $C_{17}H_{18}N_2O,0{\cdot}5H_2SO_4,H_2O$: C, 61·3; H, 6·3; N, 8·4; S, 4·8%).

5-Hydroxytryptamine (I).—Creatinine sulphate was prepared by dissolving ash-free creatinine (22·6 g.) in warm 2N-sulphuric acid (Analytical Reagent Grade, 100 ml.). The solution was clarified by filtration and poured into acetone (2 l.). The crude creatinine sulphate which separated was recrystallised (charcoal) from a mixture of ethanol (400 ml.) and water (160 ml.) to give ash-free creatinine sulphate hemihydrate (27·1 g., 80%) as prisms, m. p. (e.c.) 259—260° (decomp.) (Found: C, 28·25; H, 5·4; S, 9·2. Calc. for $C_4H_7N_3O,0{\cdot}5H_2SO_4,0{\cdot}5H_2O$: C, 28·05; H, 5·25; S, 9·4%). A suspension of 5-benzyloxytryptamine sulphate monohydrate (11·6 g., 0·035 mole) and palladised charcoal (from 0·42 g. of palladium chloride) in ethanol (180 ml.) and water (120 ml.) was hydrogenated at room temperature and 1 atm. (uptake 117%). The

[5] A. S. F. Ash, personal communication.

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catalyst and charcoal were removed by filtration through "Hyflo" and the filtrate was evaporated to a thick syrup under reduced pressure in an atmosphere of nitrogen. The syrup was dissolved in a solution of ash-free creatinine sulphate hemihydrate (5·95 g., 0·035 mole) in hot water (35 ml.) and to this solution was added hot acetone (250 ml.). The solid which separated was filtered off, washed with acetone, and dried at 80°, to give crude 5-hydroxytryptamine creatinine sulphate (13 g., 93%), m. p. (e.c.) 217—219°. This material was combined with two similar batches (total 35·8 g.), and the whole recrystallised twice by dissolution in hot water (300 ml.), filtration (charcoal), and addition of ethanol (200 ml.). 5-Hydroxytryptamine creatinine sulphate monohydrate (25·5 g., 67%) crystallised as almost colourless prisms, m. p. (e.c.) 219—221° (decomp.) (Found: C, 41·5; H, 5·7; S, 8·2, 7·9; H_2O, 4·4, 4·8. Calc. for $C_{10}H_{12}N_2O,C_4H_7N_3O,H_2SO_4,H_2O$: C, 41·5; H, 5·7; S, 7·9; H_2O, 4·45%), $\lambda_{max.}$ 275 mμ (ε 5820) at pH 7 [lit., $\lambda_{max.}$ 275 mμ (ε 5800),[4] m. p. 214—216° (Kofler) [3]].

The authors thank Dr. H. J. Barber, F.R.I.C., for his interest, Dr. D. F. Muggleton for spectra, and Mr. S. Bance, B.Sc., F.R.I.C., for microanalyses.

RESEARCH LABORATORIES, MAY AND BAKER LTD.,
DAGENHAM, ESSEX.

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561. *Derivatives of* NN-*Dialkyldiselenocarbamic Acids.*

By D. BARNARD and D. T. WOODBRIDGE.

Several sodium *NN*-dialkyldiselenocarbamates have been prepared by reaction of carbon diselenide with secondary amines in alkaline, aqueous dioxan. Treatment of solutions of these with zinc or copper sulphate yielded crystalline compounds, $[R_2N{\cdot}C(:Se){\cdot}Se{\cdot}]_2M$. Oxidation of the sodium salts under a variety of conditions gave equimolar mixtures of bis-(*NN*-dialkylselenocarbamoyl) mono- and tri- selenides rather than the expected diselenides.

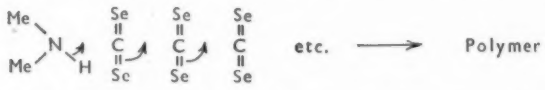
ZINC DIALKYLDITHIOCARBAMATES have been recognised recently as some of the most potent sulphur-containing antioxidants.[1] It has also been shown that the replacement of sulphur by selenium in many types of compound, particularly disulphides, often markedly increases antioxidant activity, sometimes by a factor of several hundred.[2] The synthesis of the corresponding *NN*-dialkyldiselenocarbamates was therefore of obvious interest. Bis-(*NN*-dialkylthiocarbamoyl) disulphides (tetra-alkylthiuram disulphides), the oxidation products of dialkyldithiocarbamates, are of equal importance, since, when heated with rubber in the presence of zinc oxide, they introduce mono- and di-sulphide cross-links [3,4] and at the same time produce the corresponding zinc dialkyldithiocarbamates.[5] The vulcanisates so obtained are noted for their resistance to oxidative ageing.[6] The synthesis of bis-(*NN*-dialkylselenocarbamoyl) diselenides would, by analogy, make available rubber vulcanisates which, by virtue of both selenide cross-links and accompanying diselenocarbamate, might be expected to possess even greater resistance to ageing.

Bis-(*NN*-dialkylthiocarbamoyl) disulphides, first prepared by the oxidation of ammonium or amine salts of dialkyldithiocarbamic acids,[7] are readily obtained by the oxidation of sodium dialkyldithiocarbamates (formed from carbon disulphide and a secondary amine

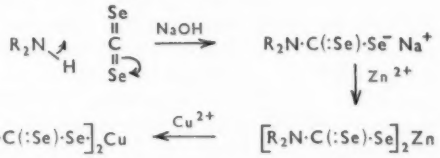
[1] Dunn and Scanlan, *Trans. Inst. Rubber Ind.*, 1958, **34**, 228.
[2] Barnard and Woodbridge, unpublished work.
[3] Studebaker and Nabors, *Rubber Chem. Tech.*, 1959, **32**, 941.
[4] Moore, *J. Polymer Sci.*, 1958, **32**, 503.
[5] Scheele, Lorentz, and Dummer, *Kautschuk u. Gummi*, 1954, **7**, WT273; *Rubber Chem. Tech.*, 1956, **29**, 1.
[6] Fletcher and Fogg, *Rubber Age*, 1959, **84**, 632.
[7] von Braun, *Ber.*, 1902, **35**, 817.

in alkaline solution) with hydrogen peroxide [8] or potassium ferricyanide.[9] Dialkyldithiocarbamates of, for example, zinc or cadmium are prepared by reaction of carbon disulphide with secondary amines in the presence of the required metal ion,[10] or from the sodium dialkyldithiocarbamate and a metal salt.[11]

The ready polymerisation of carbon diselenide, either alone [12] or in the presence of amines,[13] has been previously reported. Not unexpectedly, therefore, the addition of carbon diselenide to alkaline solutions of secondary amines, under conditions which with carbon disulphide result in quantitative yields of dithiocarbamates,[14] gave intractable dark resins. Inverse addition gave similar results and a large molar excess of carbon diselenide could be converted into polymer in this way. The resin formation is tentatively ascribed to an amine-catalysed, ionic addition polymerisation of carbon diselenide, *e.g.*:



Preparation of NN-*Dialkyldiselenocarbamates.*—Resin formation was reduced to negligible proportions by the slow addition of a dioxan solution of carbon diselenide to a vigorously stirred, alkaline solution of the secondary amine at low temperature, and high yields of the required dialkyldiselenocarbamates were thus obtained. It is apparently essential to avoid a localised excess of diselenide. Zinc dialkyldiselenocarbamates, precipitated by the addition of zinc sulphate, are stable, pale brown or yellow, crystalline materials, insoluble in water but soluble in organic solvents, their solubility increasing with the size of the alkyl groups. The intensely red copper diethyldiselenocarbamate was prepared in quantitative yield by shaking a chloroform or methylene chloride solution of the zinc derivative with aqueous copper sulphate.



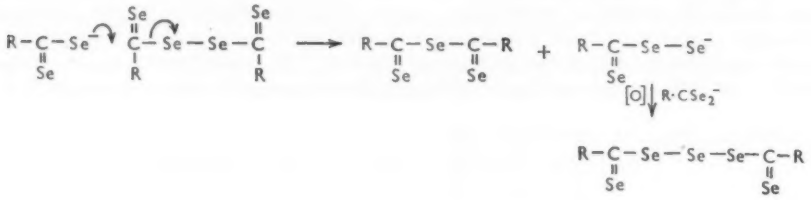
The spectra of the metal diselenocarbamates in both the visible and the ultraviolet region closely resemble those of the corresponding dithiocarbamates,[15,16] with absorption maxima similar in intensity and position except for a slight shift to longer wavelengths. The lower absorption of the copper diethyldiselenocarbamate in the visible region, $\lambda_{max.}$ 495 mμ (ε 11,780), leaves dithiocarbamates as the preferred reagents for the quantitative estimation of copper.[16]

Oxidation of sodium dialkyldiselenocarbamates gave a mixture of the bis-(*NN*-dialkylselenocarbamoyl) tri- and mono-selenides. Thus, although the theoretical quantity of oxidant was consumed and the initial product gave correct analyses for the expected diselenide, fractional crystallisation gave in each case well-defined crystalline materials (yield *ca.* 50 mole %) which contained 5 rather than 4 selenium atoms per molecule. That these contained two *NN*-dialkyldiselenocarbamoyl residues and were therefore the

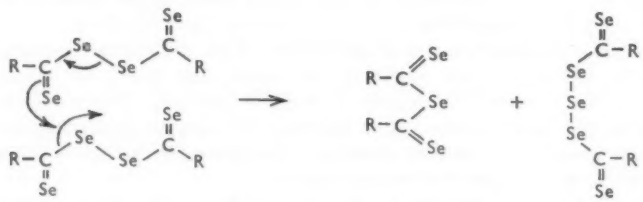
[8] Houben–Weyl, "Methoden der Organischen Chemie," Georg Thieme, Stuttgart, 1955, 4th edn., Vol. IX, p. 853.
[9] Rothstein and Binovic, *Rec. Trav. chim.*, 1954, **73**, 561.
[10] Whitby and Matheson, *Trans. Roy. Soc. Canada*, 1924, **18**, Sect. III, 111.
[11] Saville, *J.*, 1959, 2749.
[12] Ives, Pittman, and Wardlaw, *J.*, 1947, 1080.
[13] Grimm and Metzger, *Ber.*, 1936, **69**, 1356.
[14] Houben–Weyl, *op. cit.*, p. 825; Mathes, U.S.P. 2,117,619.
[15] Koch, *J.*, 1949, 401.
[16] Näsänen and Tamminen, *Suomen Kem.*, 1950, **23**, *B*, 28.

triselenides could be inferred from the almost quantitative conversion into copper *NN*-dialkyldiselenocarbamate which occurred in the presence of cupric ion and a reducing agent such as sodium thiosulphate or quinol.[11] The impure monoselenides were isolated from the mother-liquors of the fractional crystallisations.

Two possible routes to these products can be visualised. (*a*) During the oxidation the diselenide formed could be attacked by residual dialkyldiselenocarbamoyl ion:



(*b*) The diselenide could be unstable and immediately disproportionate to the mono- and tri-selenide by a mechanism such as:



The use of different oxidants, *e.g.*, hydrogen peroxide, potassium ferricyanide, or oxygen, and inversion of the normal addition of oxidant to the diselenocarbamates did not affect the composition of the products although some change might have been expected if mechanism (*a*) were operative. The disproportionation of the diselenide into mono- and tri-selenide therefore appears to be the more likely explanation.

Vulcanising and Antioxidant Properties.—Since the desired bis-(*NN*-dialkylselenocarbamoyl) diselenide was not present in the oxidation products of the selenocarbamates it was not surprising that these products had little vulcanising activity when heated with natural rubber under a wide variety of conditions.

The bis-(*NN*-dialkylselenocarbamoyl) triselenides and the metal *NN*-dialkyldiselenocarbamates were potent antioxidants for both simple olefins and rubber, the latter having a greater activity than the corresponding dithiocarbamates. Details of these results will be reported elsewhere.

Experimental

Carbon diselenide was prepared by a slight modification of the method of Ives, Pittman, and Wardlaw.[12] Methylene chloride vapour in dry nitrogen was passed through molten selenium held at 600° and the condensate distilled under reduced pressure. In a typical experiment, selenium (70 g.) gave carbon diselenide (20 g.), b. p. 45·5—46°/50 mm. (Found: C, 7·2; Se, 92·7. Calc. for CSe_2: C, 7·1; Se, 92·9%).

Reaction of Carbon Diselenide with Dimethylamine.—Carbon diselenide (2·1 g., 0·0124 mole) was added during 10 min. to a stirred solution of sodium hydroxide (0·5 g., 0·0124 mole) and dimethylamine (0·56 g., 0·0124 mole) in water (4 ml.) at −10°. An immediate precipitate of a black resin (1·30 g.), insoluble in all common solvents including boiling pyridine, was formed. Oxidation of the filtrate with 27% w/v hydrogen peroxide (0·72 ml., 0·0068 mole) in 23% w/v sulphuric acid (2·64 ml., 0·0062 mole) gave an orange solid (1·04 g., 38%), m. p. 170—210°.

Addition of carbon diselenide in excess (1·079 g., 0·00635 mole), with dioxan (10 ml.) as diluent, to a mixture of 40% dimethylamine (0·075 ml., 0·00065 mole) and sodium hydroxide

(0·0259 g., 0·00065 mole) in water (5 ml.), under the previous conditions, gave an orange-brown precipitate (0·92 g., 85% based on CSe_2), m. p. 150—170°, insoluble in all common solvents.

Optimum Conditions for the Preparation of Sodium NN-*Dialkyldiselenocarbamate Solutions.*—Carbon diselenide (2·11 g., 0·0124 mole) in dioxan (20 ml.) was added to a stirred solution of sodium hydroxide (0·5 g., 0·0124 mole) and the secondary amine (0·0124 mole) in water (20 ml.) at −10° during 30 min. in an atmosphere of nitrogen. The solution was filtered and used immediately. Addition of the amine solution to the carbon diselenide in dioxan gave a marked reduction in yield when dimethylamine was used, owing to formation of an insoluble polymer. All the following reactions were carried out with the quantities described above.

Zinc Dimethyldiselenocarbamate.—A solution of sodium dimethyldiselenocarbamate, prepared as above, was added rapidly to zinc sulphate (1·80 g., 0·0062 mole) in water (10 ml.) at 0°. The resulting precipitate was filtered off and gave a pink solid (3·03 g., 97%), m. p. 236—239°. Recrystallisation from toluene gave light brown crystals, m. p. 242—243° (Found: C, 14·95; H, 2·45; N, 5·5; Se, 63·5; Zn, 13·3; *M*, 520. $C_6H_{12}N_2Se_4Zn$ requires C, 14·6; H, 2·45; N, 5·7; Se, 64·0; Zn, 13·25%; *M*, 493·5).

Other *zinc dialkyl diselenocarbamates* were prepared in an identical manner and included:

Zinc diethyldiselenocarbamate. The precipitated yellow solid (3·07 g., 90%), m. p. 154—154·5°, was recrystallised from acetone to give a pale yellow salt, m. p. 154·5—155° (Found: C, 21·9; H, 3·85; N, 4·9; Se, 56·9; Zn, 12·1; *M*, 538. $C_{10}H_{20}N_2Se_4Zn$ requires C, 21·85; H, 3·65; N, 5·1; Se, 57·45; Zn, 11·9%; *M*, 549·5), $\lambda_{max.}$ (in methylene chloride) 285 (ε 25,850) and 317 mμ (ε 13,040).

Zinc dibutyldiselenocarbamate. The orange precipitate (2·68 g., 65%), m. p. 66—67°, gave, after recrystallisation from aqueous acetone, the pale brown salt, m. p. 68—68·5° (Found: C, 32·6; H, 5·5; N, 4·25; Se, 48·0; Zn, 9·65. $C_{18}H_{36}N_2Se_4Zn$ requires C, 32·7; H, 5·5; N, 4·25; Se, 47·8; Zn, 9·9%).

Copper Diethyldiselenocarbamate.—Zinc diethyldiselenocarbamate (0·498 g.) in chloroform (20 ml.) was shaken with copper sulphate (10 g.) in water (100 ml.). Evaporation of the deep red chloroform layer left a black solid (0·50 g., 100%), m. p. 222—223°, which gave black crystals, m. p. 225—226°, on recrystallisation from acetone–chloroform (Found: C, 22·3; H, 4·0; Se, 57·9. $C_{10}H_{20}N_2Se_4Cu$ requires C, 21·95; H, 3·7; Se, 57·65%), $\lambda_{max.}$ (in methylene chloride) 290 (ε 34,800), 324 (ε 17,120), and 495 mμ (ε 11,780).

Oxidation of Sodium Diethyldiselenocarbamate Solution.—The oxidation was carried out by using (*a*) 27% w/v hydrogen peroxide (0·72 ml., 0·0068 mole) in 23% w/v sulphuric acid (2·64 ml., 0·0062 mole) or (*b*) potassium ferricyanide (4·11 g., 0·0062 mole) in water (20 ml.), either by adding the oxidant dropwise to the standard sodium diethyldiselenocarbamate solution at −10° or by inverse addition. The products of oxidation were identical in yield, composition, and melting characteristics, 90—100% of the added oxidant being consumed in each case. The oxidation product was precipitated as an orange solid (2·50 g., 83%), m. p. 102—112° with shrinkage at 77—78° (Found: C, 24·4; H, 4·2; N, 5·7; Se, 65·8. Calc. for $C_{10}H_{20}N_2Se_4$: C, 24·8; H, 4·15; N, 5·8; Se, 65·25%). This initial product (1 g.) was separated by crystallisation from ethanol–chloroform into two components, the less soluble *bis*-(NN-*diethylselenocarbamoyl*) *triselenide* being obtained as red crystals (0·4 g.), m. p. 136—137° (Found: C, 21·3; H, 3·8; N, 5·0; Se, 70·45. $C_{10}H_{20}N_2Se_5$ requires C, 21·35; H, 3·6; N, 5·0; Se, 70·1%), $\lambda_{max.}$ 287 mμ (ε 55,200), inflexion at *ca.* 310 mμ (ε 40,500), with a second crop (0·15 g.) of m. p. 126—129°. Evaporation of the mother-liquors gave a pasty solid (0·40 g.), apparently slightly impure bis-(*NN*-diethylselenocarbamoyl) monoselenide (Found: N, 6·2; Se, 59·1. Calc. for $C_{10}H_{20}N_2Se_3$: N, 6·9; Se, 58·5%). The tri- and mono-selenide gave well-defined infrared absorption spectra almost superimposable in the region 1500—1100 cm.$^{-1}$.

Preparation of Copper Diethyldiselenocarbamate from Bis(diethylselenocarbamoyl) Triselenide.—The triselenide (0·265 g., 0·00048 mole) in chloroform (20 ml.) was shaken with sodium thiosulphate (0·28 g., 0·00096 mole) and copper sulphate (10 g.) in water (100 ml.), the wine-red chloroform layer being separated at once. On evaporation a black solid (0·203 g., 77%), m. p. 215—220°, was obtained, which after recrystallisation from acetone–chloroform had m. p. and mixed m. p. with copper diethyldiselenocarbamate 224·5—226°.

The yield was also determined spectrophotometrically. The triselenide (10 mg.) in methylene chloride (25 ml.) was shaken with copper sulphate (0·88 g.) and sodium thiosulphate (11·9 mg.) in water (25 ml.) for 10 sec. The organic layer was immediately separated and diluted, and the absorption at 495 mμ determined. The yield was 88%. In the absence of thiosulphate

the colour developed very slowly and after 20 hr. the yield was 62%; in the presence of quinol (11 mg.), after 2 hr. the yield was 79%. A complicating factor was the rapid destruction of the compound by thiosulphate ion in the presence of excess of cupric ion with the formation of an insoluble brown gum. The monoselenide gave the copper diethyldiselenocarbamate in 51 mole % yield, estimated spectrophotometrically, under identical conditions.

Bis(dimethylselenocarbamoyl) Triselenide.—The orange solid (2·67 g., 99%) initially obtained from sodium dimethyldiselenocarbamate (0·0124 mole) by oxidation with hydrogen peroxide as above had m. p. 200—210° with shrinkage at 170° (Found: C, 17·2; H, 2·9; Se, 73·1. Calc. for $C_6H_{12}N_2Se_4$: C, 16·8; H, 2·8; Se, 73·8%). Crystallisation from chloroform gave the red *triselenide*, m. p. 223—224° (Found: C, 14·4; H, 2·3; N, 5·65; Se, 77·0. $C_6H_{12}N_2Se_5$ requires C, 14·2; H, 2·4; N, 5·55; Se, 77·9%).

Bis-(NN-dibutylselenocarbamoyl) Triselenide.—Oxidation of sodium dibutyldiselenocarbamate (0·0124 mole) gave a black oil (2·83 g., 76%) from which, after several recrystallisations from ethanol at low temperature, was isolated an orange solid *triselenide* (0·56 g.), m. p. 39—40° (Found: C, 32·1; H, 5·3; N, 4·2; Se, 58·8. $C_{18}H_{36}N_2Se_5$ requires C, 32·05; H, 5·4; N, 4·15; Se, 58·45%).

NN-*Dimethyldiselenocarbamic Acid.*—A solution of sodium dimethyldiselenocarbamate (0·0124 mole) was acidified with dilute sulphuric acid, and the resulting orange precipitate (1·60 g.; m. p. 98—105°) filtered off in the absence of air (Found: C, 15·65; H, 3·3; N, 6·1; Se, 74·8. $C_3H_7NSe_2$ requires C, 16·8; H, 3·3; N, 6·5; Se, 73·4%). This *acid* was soluble in alkali and oxidised in the air to an orange solid, m. p. 190—210°, from which bis(dimethyldiselenocarbamoyl) triselenide, m. p. and mixed m. p. 223—224°, was obtained by recrystallisation from chloroform or pyridine.

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WELWYN GARDEN CITY, HERTS.

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562. *The Cross-linking of Cellulose and its Derivatives. Part II.*[1] *Preparation of Some New Amino-derivatives of* D-*Glucose and of* D-*Galactose.*

By W. M. CORBETT.

With methanolic ammonia 6-deoxy-6-iododi-*O*-isopropylidene-D-galactose gives mainly 6-deoxydi-*O*-isopropylidene-6-methylamino-D-galactose whereas use of aqueous ammonia gives the tertiary amine with three sugar residues and use of ammonia in dioxan gives the latter and the secondary amine. 2-Aminoethyl ethers of di-*O*-isopropylidene-D-glucose and -D-galactose have been prepared from the corresponding methoxycarbonylmethyl ethers. These were converted into the amides which were then reduced to the amines. 3-Aminopropyl ethers were also prepared by reduction of the 2-cyanoethyl ethers.

IN Part I[1] the addition of amines to unsaturated cellulose esters was outlined as a useful means of cross-linking cellulose and its derivatives. Such a reaction, however, can only be used if its chemistry is known in detail. Because of the impossibility of following reactions of cellulose derivatives in which only a few repeating units are involved, it is necessary to determine the details by using model compounds. That work is reported in the following paper. For the study to be complete, use of amino-derivatives of monosaccharides is essential, but only a few of these compounds have been previously reported. This paper describes the preparation of free amino-derivatives of monosaccharides by simple methods which can be applied to cellulose.

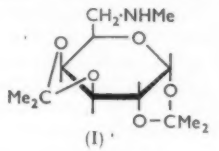
The toluene-*p*-sulphonyl group is capable of exchange by several reagents, but with ammonia it appears that formation of an anhydro-sugar intermediate is essential for high

[1] Part I, Corbett and McKay, *J. Soc. Dyers and Colourists*, in the press.

yield. Since this would impose severe restrictions in the case of cellulose derivatives, attention was turned to the replacement of iodo-groups by ammonia. 6-Deoxy-6-iododi-*O*-isopropylidene-D-galactose was studied because of its ease of preparation. Treatment with methanolic ammonia at 130° gave a syrup which was mainly 6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-methylamino-D-galactose (I) contaminated with 6-amino-6-deoxydi-*O*-isopropylidene-D-galactose. The syrup gave the picrolonate of the *N*-methyl derivative in 61% yield, whereas with phenyl isocyanate the corresponding asymmetrical disubstituted urea from the free amino-derivative was obtained in 34% yield. The *N*-methyl derivative was probably formed by reaction of the hydriodide of the primary amine with the solvent. Aqueous ammonia was then used in an attempt to overcome the participation of the solvent, but the only product isolated was 6,6′,6″-nitrilotri-(6-deoxydi-*O*-isopropylidene-D-galactose), *i.e.*, the tertiary amine (II). This, together with the secondary amine analogue (III), was also isolated after reaction of ammonia in dioxan with the iodide.

A study of the reactions of 3-*O*-2′-iodoethyldi-*O*-isopropylidene-D-glucose had to be abandoned because of the low yield of 3-*O*-2′-hydroxyethyldi-*O*-isopropylidene-D-glucose obtained by reaction of 2-chloroethanol with di-*O*-isopropylidene-D-glucose.

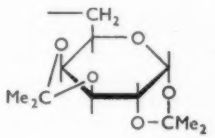
Introduction of a primary amine group has been achieved by starting from the methoxycarbonylmethyl ethers of 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose and 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose. These are prepared by treating the sodium salt of the sugar derivative with methyl halogenoacetate as described by Shyluk and Timell.[2] 1,2:5,6-Di-*O*-isopropylidene-3-*O*-methoxycarbonylmethyl-D-glucofuranose (IV) is readily converted into the corresponding amide (V) by aqueous ammonia, and this is reduced by lithium aluminium hydride, in high yield, to 3-*O*-2′-aminoethyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (VI). The same series of reactions has been successfully applied to 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose, but in this case the initial methyl ester is a syrup and is difficult to purify: it led to the isolation of di-*O*-isopropylidene-D-galactose and of glycine amide hydrochloride as well as of the amide of the galactose derivative.

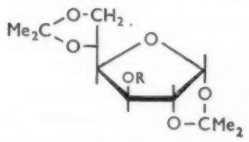


(I)

R_3N and R_2NH where R =

(II) (III)





R		R	
(IV)	$CH_2·CO_2Me$	(VII)	$CH_2·CH_2·CN$
(V)	$CH_2·CO·NH_2$	(VIII)	$CH_2·CH_2·CH_2·NH_2$
(VI)	$CH_2·CH_2·NH_2$		

The use of acrylonitrile has also been examined. 1,2:5,6-Di-*O*-isopropylidene-D-glucofuranose reacted with acrylonitrile in the presence of sodium methoxide to give in low yield 3-*O*-2′-cyanoethyldi-*O*-isopropylidene-D-glucofuranose (VII) as a liquid which was difficult to purify. Attempted reduction of the cyanoethyl ether with lithium aluminium hydride caused cleavage of the cyanoethyl group, and di-*O*-isopropylidene-D-glucose was isolated in high yield. However, reduction by hydrogen over Raney nickel gave the amine (VIII) smoothly. Di-*O*-isopropylidene-D-galactopyranose behaved similarly except that the 2′-cyanoethyl ether was obtained in a higher yield and was readily purified by distillation.

Experimental

Reactions of 6-Deoxy-6-iodo-1,2:3,4-di-O-isopropylidene-D-galactose.—(a) *With methanolic ammonia.* The iodo-derivative (4·742 g.) in methyl alcohol (200 ml.) previously saturated

[2] Shyluk and Timell, *Canad. J. Chem.*, 1956, **34**, 575.

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at 0° with ammonia was heated at 130° for 18 hr. Concentration of the solution gave a brown syrup (6·806 g.) which partly crystallised from ethyl acetate, to give ammonium iodide. The ethyl acetate solution was concentrated to a syrup (5·027 g.) which was dissolved in chloroform, then washed with aqueous sodium thiosulphate followed by water, dried (Na_2SO_4), treated with charcoal, and concentrated to a pale brown syrup (3·147 g.). It was mainly 6-*deoxy*-1,2:3,4-*di*-O-*isopropylidene*-6-*methylamino*-D-*galactopyranose* and had b. p. 140°/0·01 mm. (bath-temp.), n_D^{23} 1·4710, $[\alpha]_D^{25}$ −63·8° (*c* 0·97 in chloroform) (Found: C, 57·0; H, 8·4; N, 5·0%). It was redistilled, the bulk having b. p. 125°/0·02 mm. (bath-temp.) (Found: C, 57·2; H, 8·4; N, 5·2; NMe, 3·1. $C_{13}H_{23}NO_5$ requires C, 57·2; H, 8·5; N, 5·1; NMe, 11·2%).

The syrup (0·425 g.) gave with picrolonic acid (0·433 g.) in ethyl alcohol (10 ml.) the *amine picrolonate* (0·513 g., 61%), m. p. 233° (decomp.) (from ethyl alcohol) (Found: C, 51·3; H, 5·9; N, 12·3. $C_{23}H_{31}N_5O_{10}$ requires C, 51·4; H, 5·8; N, 13·0%). In contrast the syrup (0·282 g.) gave with phenyl isocyanate the N′-*phenylurea derivative* (0·138 g., 34%), m. p. 153° (from aqueous alcohol) (Found: C, 60·4; H, 7·1; N, 7·2. $C_{19}H_{26}N_2O_6$ requires C, 60·3; H, 7·0; N, 7·4%).

(b) *With aqueous ammonia.* The iodo-derivative (2·000 g.) was heated with aqueous ammonia (50 ml.; *d* 0·9) for 5 hr. at 110°. The mixture was extracted with chloroform, and the extract dried (Na_2SO_4) and concentrated to a syrup (1·504 g.) which crystallised from light petroleum (b. p. 40—60°). 6,6′,6″-*Nitrilotri*-(6-*deoxy*-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose*) (II) (0·596 g.), m. p. 207—210° (decomp.), had, after two recrystallisations from aqueous alcohol, m. p. 239—240° (decomp.), $[\alpha]_D^{21}$ −56·0° (*c* 0·5 in chloroform) [Found: C, 58·0; H, 7·7; N, 1·6%, *M* (Rast), *ca.* 800. $C_{36}H_{57}NO_{15}$ requires C, 58·2; H, 7·7; N, 1·9%; *M*, 743]. Further material was isolated from the petroleum mother-liquors.

(c) *With ammonia in dioxan.* The iodo-derivative (5·320 g.) in dioxan (200 ml.), previously saturated at 0° with ammonia, was heated at 130° for 5½ hr. The mixture was concentrated under reduced pressure and the residue dissolved in chloroform, washed with water, dried (Na_2SO_4), treated with charcoal, and concentrated to a brown syrup (2·656 g.). This partly crystallised from aqueous alcohol to give crystals which after one recrystallisation from aqueous alcohol had m. p. 211° and an infrared spectrum identical with that of the product obtained as in (b).

The aqueous-alcohol solution was concentrated and a sample of the syrup (0·965 g.) in a little ether was chromatographed on alumina (40 × 1·3 cm.). Elution with a mixture of light petroleum (b. p. 40—60°; 300 ml.) and ether (600 ml.), followed by chloroform (300 ml.), gave an amorphous mass (0·371 g.) which crystallised from di-isopropyl ether to give material of m. p. 129—131°. The chloroform eluate gave further crystals (0·201 g.), m. p. 126·5—128·5°. The two fractions were combined and recrystallised twice from di-isopropyl ether to give 6,6′-iminodi-(6-deoxydi-*O*-isopropylidene-D-galactopyranose (III), m. p. 130—131°, $[\alpha]_D^{21}$ −81·2° (*c* 0·8 in chloroform) {Freudenberg and Doser [3] give m. p. 125—126°, $[\alpha]_{378}^{18}$ −84·4° (in acetone)} [Found: C, 57·8; H, 8·0; N, 2·4%; *M* (Rast), *ca.* 445. Calc. for $C_{24}H_{39}NO_{10}$: C, 57·6; H, 7·9; N, 2·8%; *M*, 501].

3-O-2′-*Hydroxyethyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose*.—To the sodium salt of 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (25·0 g.) in light petroleum (b. p. 60—80°; 150 ml.) was added 2-chloroethanol (8 ml.). After the vigorous exothermic reaction had subsided, the mixture was refluxed for 2 hr., and then chloroform was added. The solid material was filtered off, and the filtrate concentrated (charcoal) to a syrup which crystallised from light petroleum (b. p. 60—80°) to give di-*O*-isopropylidene-D-glucose (15·7 g.). Concentration of the mother-liquors gave a golden syrup (6·1 g.) which distilled at 125°/0·005 mm. (bath-temp.). The 3-O-2′-*hydroxyethyl ether* had $[\alpha]_D^{21}$ −2·2° (*c* 1·4 in chloroform), n_D^{21} 1·4710 (Found: C, 55·7; H, 7·9. $C_{14}H_{24}O_7$ requires C, 55·3; H, 8·0%).

3-O-*Carbamoylmethyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose*.—1,2:5,6-Di-*O*-isopropylidene-3-*O*-methoxycarbonylmethyl-D-glucose [2] (2·2 g.) was suspended in aqueous ammonia (100 ml.), dissolving in 4 hr. The solution was concentrated under reduced pressure to a syrup. This crystallised, and after digestion with light petroleum (b. p. 40—60°) the *amide* (1·8 g.; m. p. 100—102°) after several recrystallisations from di-isopropyl ether, had m. p. 104·5—105·5°, $[\alpha]_D^{21}$ −67·8° (*c* 2·0 in chloroform) (Found: C, 53·2; H, 7·4; N, 4·5. $C_{14}H_{23}NO_7$ requires C, 53·1; H, 7·3; N, 4·4%).

3-O-2′-*Aminoethyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose*.—To a solution of the above

[3] Freudenberg and Doser, *Ber.*, 1925, **58**, 294.

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amide (1·807 g.) in dry ether (50 ml.) was slowly added with stirring an ether suspension of lithium aluminium hydride (2·95 g.). The stirring was continued for 18 hr., then the excess of hydride was decomposed by ethyl acetate, and the mixture concentrated. The residue was extracted with chloroform, and the extract concentrated to a brown syrup (1·474 g.). Distillation gave 3-O-2′-*aminoethyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose* (0·587 g.), b. p. 140°/0·005 mm. (bath-temp.), n_D^{21} 1·4660, $[\alpha]_D^{22}$ −36·0° (*c* 1·0 in ethanol) (Found: C, 55·8; H, 8·4; N, 4·1. $C_{14}H_{25}NO_6$ requires C, 55·5; H, 8·3; N, 4·6%).

1,2:3,4-*Di*-O-*isopropylidene*-6-O-*methoxycarbonylmethyl*-D-*galactose*.—To the sodium salt of 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (20·3 g.) in light petroleum (b. p. 60—80°) was added methyl chloroacetate (14 ml., 1·22 equiv.), and the mixture heated at 70° for 2 hr. before being diluted with chloroform. The mixture was then washed with water, treated with charcoal, dried (Na_2SO_4), and concentrated to a brown syrup. This was distilled to give the *ester-ether* (13·6 g.), b. p. 110—112°/0·01 mm., n_D^{24} 1·4673, $[\alpha]_D^{24}$ −57·8° (*c* 1·5 in chloroform) (Found: C, 54·2; H, 7·4. $C_{15}H_{24}O_8$ requires C, 54·3; H, 7·3%).

6-O-*Carbamoylmethyl*-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose*.—The galactose ester (7·139 g.) was dissolved in aqueous ammonia (100 ml.; *d* 0·9) and after 3 hr. at room temperature there separated needles, m. p. 125—127°. The *amide* (2·396 g.), after one recrystallisation from ethanol–di-isopropyl ether, had m. p. 126·5—128°, $[\alpha]_D^{21}$ −97·0° (*c* 0·95 in chloroform) (Found: C, 53·1; H, 7·3; N, 4·6. $C_{14}H_{23}NO_7$ requires C, 53·1; H, 7·3; N, 4·4%).

The ammoniacal liquors were concentrated and the residue digested with ethanol–di-isopropyl ether. The residue partly crystallised from aqueous acetone to give glycine amide hydrochloride, m. p. 215—217°. Bergell and van Wülfing [4] give m. p. 186—189° (Found: C, 21·7; H, 6·6; N, 25·1; Cl, 31·1. Calc. for $C_2H_7ClN_2O$: C, 21·7; H, 6·4; N, 25·3; Cl, 32·1%).

Concentration of the ethanol–di-isopropyl ether mother-liquors gave a syrup (3·671 g.), b. p. 150—170°/0·005 mm. (bath-temp.), n_D^{21} 1·4690, $[\alpha]_D^{25}$ −61·5° (*c* 1·6 in chloroform). It was impure di-*O*-isopropylidene-D-galactose (Found: C, 55·3; H, 8·0; N, 0·8; OMe, 0·3. Calc. for $C_{12}H_{20}O_6$: C, 55·5; H, 7·8%).

6-O-2′-*Aminoethyl*-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose*.—The galactose amide (2·419 g.) was reduced with lithium aluminium hydride (4·12 g.), to give the *aminoethyl ether* (0·903 g.), b. p. 145°/0·01 mm. (bath-temp.), n_D^{17} 1·4683 (Found: C, 55·8; H, 8·6; N, 4·1. $C_{14}H_{25}NO_6$ requires C, 55·5; H, 8·3; N, 4·6%).

3-O-2′-*Cyanoethyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose*.—To di-*O*-isopropylidene-D-glucose (7·716 g.) in dry dioxan (10 ml.) was added with stirring sodium methoxide (*ca.* 0·2 g.) followed by acrylonitrile (3 ml.). The stirring was continued for 19 hr. at 60° and then the mixture was diluted with chloroform. The solution was washed with dilute sulphuric acid, aqueous sodium hydrogen carbonate, and finally water, dried (Na_2SO_4), and concentrated to a clear syrup (6·760 g.). This was fractionally distilled to give two fractions. The first (3·269 g.), b. p. 120—124°/0·01 mm., crystallised from light petroleum (b. p. 60—80°) to give di-*O*-isopropylidene-D-glucose, m. p. and mixed m. p. 103—108·5°. The second fraction (1·632 g.), b. p. 128—140°/0·01 mm., had n_D^{20} 1·4630, $[\alpha]_D^{20}$ −24·3° (*c* 2·8 in chloroform), and was 3-O-2′-*cyanoethyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose* (Found: C, 57·6; H, 7·6; N, 4·3. $C_{15}H_{23}NO_6$ requires C, 57·6; H, 7·4; N, 4·5%).

3-O-3′-*Aminopropyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucosefuranose*.—Reduction of the cyanoethyl ester in ether solution with lithium aluminium hydride gave di-*O*-isopropylidene-D-glucose in 73% yield. A solution of the impure cyanoethyl ether (8·0 g.) in dry methanol was hydrogenated for 2 hr. over Raney nickel (0·5 g.) at 130°/130 atm. The cooled mixture was filtered, and the filtrate concentrated to a syrup which was distilled, to give the *aminopropyl ether* (3·2 g.), b. p. 130—140°/0·005 mm., n_D^{23} 1·4649, $[\alpha]_D^{22}$ −33·4° (*c* 1·2 in chloroform) (Found: C, 56·6; H, 8·8; N, 3·1. $C_{15}H_{27}NO_6$ requires C, 56·8; H, 8·6; N, 4·4%).

6-O-2′-*Cyanoethyl*-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose*.—Di-*O*-isopropylidene-D-galactose (12·652 g.) was treated with acrylonitrile (6 ml.) to give the *cyanoethyl ether* (10·661 g.), b. p. 138°/0·005 mm., n_D^{20} 1·4670, $[\alpha]_D^{21}$ −62·9° (*c* 1·7 in chloroform) (Found: C, 57·6; H, 7·6; N, 4·6. $C_{15}H_{23}NO_6$ requires C, 57·6; H, 7·4; N, 4·5%).

6-O-3′-*Aminopropyl*-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose*.—Reduction of the galactose cyanoethyl ether in ether solution with lithium aluminium hydride gave di-*O*-isopropylidene-D-galactose in 99% yield. A solution of the ether (34·36 g.) in dry methanol was hydrogenated over Raney nickel (1·0 g.) at 130°/130 atm. of hydrogen for 2 hr. The *aminopropyl*

[4] Bergell and van Wülfing, *Z. physiol. Chem.*, 1910, **64**, 353.

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ether produced was fractionally distilled to give fraction (*a*) (11·83 g.), b. p. 130°/0·005 mm., n_D^{22} 1·4690, $[\alpha]_D^{23}$ −60·5° (*c* 1·0 chloroform) (Found: C, 56·4; H, 8·5; N, 3·9. $C_{15}H_{27}NO_6$ requires C, 56·8; H, 8·6; N, 4·4%), and fraction (*b*) (13·47 g.), b. p. 135°/0·01 mm., n_D^{22} 1·4680, $[\alpha]_D^{23}$ −67·5° (*c* 1·0 in chloroform) (Found: C, 56·7; H, 8·7; N, 4·3%).

Acknowledgment is made to Mr. A. T. Masters for microanalyses and to Mr. D. Winters for experimental assistance.

British Rayon Research Association, Heald Green Laboratories, Wythenshawe, Manchester, 22.
[Present address: Imperial Chemical Industries Ltd., Fibres Division, Harrogate, Yorks.]
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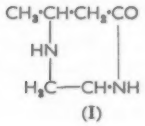
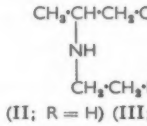
563. *The Cross-linking of Cellulose and its Derivatives. Part III.*[1] *The Addition of Amines to Crotonyl Esters.*

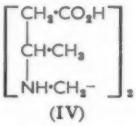
By W. M. Corbett and J. E. McKay.

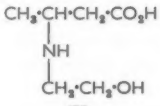
The addition of some primary aliphatic amines to ethyl crotonate and 1,2:5,6-di-*O*-isopropylidene-D-glucose 3-crotonate, and of this sugar ester to amino-derivatives of simple sugars, has been investigated; the products have been identified as far as possible.

The general purport of this work has been previously described,[1] stress being laid on the possible value of addition of amines to crotonyl esters of cellulose in the formation and estimation of cross-links. Although this reaction has already been used to induce insolubility in cellulose crotonates,[2] the process of cross-linking has been inferred to occur by β-addition of a diamine to the double bonds without formal corroboration. From the work of Stadnikow [3] and Morsch [4] it is known that crotonates add the elements of ammonia and simple amines to form β-amino- and β-alkylamino-butyrates as well as the corresponding amides, the relative contributions of addition and aminolysis depending on the conditions. The object of the present work, therefore, has been to determine the validity of applying this reaction to carbohydrate derivatives and to establish, for analytical purposes, the structures of the cross-links formed between molecules.


(I)


(II; R = H) (III; R = Ac)


(IV)

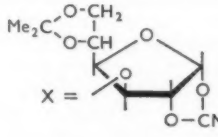

(V)

We first studied the reaction between methyl crotonate and ethylenediamine. At temperatures significantly above 20° aminolysis leads to a complex mixture from which β-*N*-2′-aminoethylaminobutyric lactam (I) was isolated; this was hydrolysed by hydrochloric acid to the acid (II), which was isolated as the crystalline dihydrochloride. This compound is more satisfactorily obtained by addition of *N*-acetylethylenediamine to ethyl crotonate at lower temperatures and subsequent saponification of the product (III). The product (IV) of diaddition, being crystalline, is readily isolated from the low-temperature reaction between ethylenediamine and ethyl crotonate.

The addition to 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose 3-crotonate (VI) was next examined. Ethanolamine had been found to add to crotonic acid *via* the ammonium salt to form the acid (V), and with the sugar crotonate it gave a product that on hydrolysis

[1] Part I, Corbett and McKay, *J. Soc. Dyers and Colourists*, in the press; Part II, preceding paper.
[2] Engelmann and Exner, *Makromol. Chem.*, 1957, **23**, 233.
[3] Stadnikow, *Ber.*, 1911, **44**, 52; *J. Russ. Phys. Chem. Soc.*, 1909, **41**, 900; 1910, **42**, 885.
[4] Morsch, *Monatsh.*, 1932, **60**, 50.

yielded 1,2:5,6-di-*O*-isopropylidene-D-glucose (VII) and the same acid (V). The addition compound can thus be represented as the aminobutyrate (VIII). There is no addition of ethanolamine or ammonia to the 3-but-2′-enyl or 3-allyl ether of di-*O*-isopropylidene-D-glucose. The 3-acetate is also not attacked by ethanolamine during 18 hr. at room



(VI) X·CO·CH:CHMe

(VII) XH

(VIII) X·CO·CH$_2$·CHMe·NH·CH$_2$·CH$_2$·OH

(IX) X·CH$_2$·CH$_2$·NH$_2$

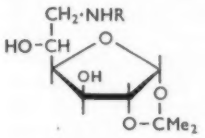
X·CH$_2$·CH$_2$·NH·CHMe·CH$_2$·CO·X (X)

X·CH$_2$·CH$_2$·CH$_2$·NH$_2$ (XI)

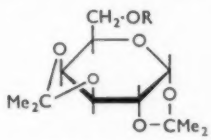
temperature, suggesting that little aminolysis of unsubstituted crotonyl groups occurs and that addition is to the sugar ester and not to liberated crotonamide. Reaction between the sugar crotonate (VI) and ethylenediamine yields the addition product (XV), since it gives on hydrolysis the glucofuranose derivative (VII) and the diacid (IV).

We then studied a case where the amine was itself a sugar derivative. 6-Amino-6-deoxy-1,2-*O*-isopropylidene-D-glucofuranose (XII) was treated with the sugar crotonate (VI) and from the products a component was isolated whose analyses corresponded to those of the disugar compound (XIII). Hydrolysis of this yielded the component sugar (VII) and the carbohydrate amino-acid derivative (XIV).

Reaction of 3-*O*-2′-aminoethyl-1,2:5,6-di-*O*-isopropylidene-D-glucose (IX) with the sugar crotonate (VI) gave a product with an analysis corresponding to the adduct (X), but because of the small amount available, the only crystalline material which could be isolated after hydrolysis was the component (VII). The same behaviour was observed



X as above



(XII) R = H

(XIII) R = CHMe·CH$_2$·CO·X

(XIV) R = CHMe·CH$_2$·CO$_2$H

X·CO·CH$_2$·CHMe·NH·CH$_2$·CH$_2$·NH·CHMe·CH$_2$·CO·X (XV)

(XVI) R = CH$_2$·CH$_2$·NH$_2$

(XVII) R = CH$_2$·CH$_2$·CH$_2$·NH$_2$

(XVIII) R = CH$_2$·CH$_2$·NH·CHMe·CH$_2$·CO$_2$H

(XIX) R = CH$_2$·CH$_2$·CH$_2$·NH·CHMe·CH$_2$·CO$_2$H

with the more readily available 3-*O*-3′-aminopropyl derivative (XI). When the amines (XVI) and (XVII) reacted with the crotonate (VI), not only did the products give correct analyses for the addition compounds but on hydrolysis they yielded, in addition to the component (VII), crystalline compounds corresponding in analysis to the acid components (XVIII) and (XIX),

It is evident that these three types of reaction are capable of forming bridges between pairs of carbohydrate molecules. It is true that the glucose and galactose derivatives used cannot be regarded as exactly analogous to the substituted glucoses in cellulose derivatives. Nevertheless, the addition occurs readily in the face of considerable steric opposition by the isopropylidene substituents and should not be greatly hindered when applied to cellulosic systems.

Experimental

Addition of Ethylenediamine to Methyl Crotonate at 65°.—To a refluxing solution of ethylenediamine (60 g.) in methanol (200 ml.) in an atmosphere of nitrogen methyl crotonate (100 g.) in methanol (100 ml.) was added dropwise, during 5 hr. Refluxing was continued for a further 24 hr., and then the solvent was removed by distillation to leave a colourless syrup. Repeated sublimation of the syrup, or exhaustive extraction with benzene followed by recrystallisation of

the extract from ethyl acetate containing a little methanol, gave colourless needles of β-2′-*aminoethylaminobutyric lactam* (I) (17 g., 13%), m. p. 113—114° (Found: C, 56·6; H, 9·2; N, 21·6. $C_6H_{12}N_2O$ requires C, 56·2; H, 9·4; N, 21·9%), that gave a *picrate*, m. p. 242° (Found: C, 40·4; H, 4·3; N, 19·6. $C_{12}H_{15}N_5O_8$ requires C, 40·4; H, 4·2; N, 19·6%), and an *acetate*, needles, m. p. 100—101° (Found: C, 56·8; H, 8·3; N, 16·2. $C_8H_{14}N_2O_2$ requires C, 56·6; H, 8·3; N, 16·4%).

A solution of the lactam (2 g.) in 10% hydrochloric acid (35 ml.) was refluxed for 4 hr. and then concentrated. Recrystallisation of the residue from ethanol–ether gave needles of β-2′-*aminoethylaminobutyric acid dihydrochloride* (as II) (2 g.), m. p. 150—151° (Found: C, 32·8; H, 7·4; Cl, 33·7; N, 12·8. $C_6H_{16}Cl_2N_2O_2$ requires C, 32·9; H, 7·3; Cl, 32·7; N, 12·8%). This was converted into the syrupy free amine by treatment with Amberlite IR-4B (OH) resin. Esterification with ethanolic hydrogen chloride gave the *ester dihydrochloride*, m. p. 111° (from benzene–ethanol), and showing evidence of hydration in the infrared spectrum (Found: C, 38·1; H, 8·0; Cl, 27·8. $C_8H_{20}Cl_2N_2O_2,\frac{1}{2}H_2O$ requires C, 37·7; H, 8·2; Cl, 27·7%).

Addition of Ethylenediamine to Ethyl Crotonate at 4°.—A solution of ethyl crotonate (30 g.) and ethylenediamine (8 g.) in ethanol (100 ml.) was kept at 4° for 5·5 days. Ethanol and unchanged amine were removed by evaporation and the residue heated with water for 2 hr. Concentration of the solution gave a syrup which gave crystals from ethanol–ether. After one recrystallisation from aqueous ethanol the *NN′-ethylenedi-*(β-*aminobutyric acid*) (IV) (5·5 g., 18%) had m. p. 216—218° (Found: C, 51·5; H, 8·5; N, 12·2. $C_{10}H_{20}N_2O_4$ requires C, 51·8; H, 8·6; N, 12·1%), that gave a *dipicrate*, m. p. 205—206° (Found: C, 38·2; H, 3·8; N, 16·2. $C_{30}H_{26}N_8O_{18}$ requires C, 38·2; H, 3·8; N, 16·2%), a dark blue *copper salt* (Found: C, 40·9; H, 6·5; Cu, 21·1; N, 9·2. $C_{10}H_{18}CuN_2O_4$ requires C, 40·9; H, 6·2; Cu, 21·7; N, 9·6%), and a *diethyl ester dihydrochloride*, m. p. 194—195° (Found: C, 46·8; H, 8·4; N, 7·8. $C_{14}H_{30}Cl_2N_2O_4$ requires C, 46·5; H, 8·3; N, 7·8%).

Addition of N-*Acetylethylenediamine to Ethyl Crotonate at* 4°.—A solution of mono-*N*-acetylethylenediamine [5] (18·5 g.) and ethyl crotonate (18·5 g.) in ethanol (70 ml.) was kept at 4° for 6 days. A small amount of solid, m. p. 293° (decomp.), which separated was removed and the solution concentrated to retain the components of b. p. >80°. This residue was dissolved in water and extracted with ether to remove unchanged ethyl crotonate (2—3 g.). The aqueous phase was evaporated to a syrup which yielded microcrystals from ethanol–ether. After two recrystallisations β-2′-*acetylamidoethylaminobutyric acid* (III) (17·5 g., 55%) had m. p. 158—160° (Found: C, 51·0; H, 8·5; N, 14·7. $C_8H_{16}N_2O_3$ requires C, 51·1; H, 8·5; N, 14·9%).

The acetyl derivative (2 g.) was treated for 3 hr. with 5% boiling aqueous potassium hydroxide (100 ml.), then the solution was neutralised with carbon dioxide and evaporated. The residue was extracted with ethanol and the extract evaporated to dryness, treated with hydrochloric acid, and evaporated again. This residue was also extracted with alcohol. Addition of chloroform to this extract gave colourless crystals of β-2′-*aminoethylaminobutyric acid dihydrochloride*. After two recrystallisations from ethanol–acetone, the salt (0·9 g., 39%) had m. p. 151—152° (Found: C, 32·6; H, 7·6; N, 12·4. $C_6H_{16}Cl_2N_2O_2$ requires C, 32·9; H, 7·3; N, 12·8%). Addition of ether to the mother-liquors yielded crystals; after three recrystallisations from ethanol–ether the *ethyl* β-2′-*aminoethylaminobutyrate dihydrochloride* (1·4 g., 40%) had m. p. 111—112° (Found: C, 37·8; H, 8·2; N, 11·1. $C_8H_{20}Cl_2N_2O_2,\frac{1}{2}H_2O$ requires C, 37·7; H, 8·2; N, 10·9%).

Addition of Ethanolamine to Crotonic Acid.—To a solution of crotonic acid (4 g.) in ethanol (50 ml.) was added ethanolamine (3 ml.). After 18 hr. at room temperature the solution was concentrated to give white crystals, m. p. 88—91°. Recrystallisation from acetone–light petroleum (b. p. 40—60°) afforded 2-*hydroxyethylammonium crotonate* (4·6 g., 69%), m. p. 85—90° (Found: C, 49·0; H, 9·0; N, 9·5. $C_6H_{13}NO_3$ requires C, 49·0; H, 8·9; N, 9·5%).

The salt took up 4·80, 4·85, 5·35, and 5·88 moles of oxygen in $\frac{1}{4}$, $\frac{1}{2}$, 1, and 5 hr., respectively, when oxidised with acidic permanganate at 23°. On long standing, or on heating at 100° for 1 hr., the salt reverted to a pale brown syrup which, after extraction with acetone, left a residue. This recrystallised from ethanol–light petroleum (b. p. 40—60°) to give β-2′-*hydroxyethylaminobutyric acid* (V), m. p. 181·5—183·5° (Found: C, 49·4; H, 9·1; N, 9·6. $C_6H_{13}NO_3$ requires C, 49·0; H, 8·9; N, 9·5%).

In contrast *ethylenediammonium crotonate*, m. p. 121·5—122·5°, is stable on storage and at 100° (Found: C, 51·8; H, 8·8; N, 12·0. $C_{10}H_{20}N_2O_4$ requires C, 51·8; H, 8·6; N, 12·1%).

[5] Hill and Aspinall, *J. Amer. Chem. Soc.*, 1939, **61**, 822.

1,2:5,6-*Di*-O-*isopropylidene*-D-*glucofuranose* 3-*Crotonate* (VI) (with Mr. J. A. D. EWART).—The crotonate is obtained by treating the sodium salt of di-*O*-isopropylidene-D-glucofuranose with crotonyl chloride, or di-*O*-isopropylidene-D-glucopyranose with crotonic anhydride and pyridine. The *crotonate* product was best purified by distillation under a high vacuum and then readily crystallised, having m. p. 65·5—67°, $[\alpha]_D^{22}$ −48·4° (*c* 4·7 in chloroform) (Found: C, 58·5; H, 7·4; OCr, 21·2. $C_{16}H_{24}O_7$ requires C, 58·5; H, 7·4; OCr, 21·0%).

3-O-*But*-2′-*enyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose*.—The di-*O*-isopropylidene-D-glucofuranose (1·0 g.), powdered sodium hydroxide (0·4 g.), and dioxan (5 ml.) were stirred at 45° whilst but-2-enyl bromide (4 ml.) was added during 20 min. The mixture was heated with stirring for 1½ hr. at 50°, and then 3 hr. at 55—60°. Water was added, and the mixture extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and concentrated to a liquid (1·2 g., 104%) which distilled at 120°/0·02 mm. (bath-temp.). The *ether* had n_D^{21} 1·4602, and $[\alpha]_D^{20}$ −18·8° (*c* 1·3 in chloroform) (Found: C, 61·1; H, 8·4. $C_{16}H_{26}O_6$ requires C, 61·2; H, 8·4%).

3-O-*Allyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose*.—The *allyl ether* was prepared similarly to the butenyl ether and had b. p. 113°/0·005 mm. (bath-temp.), n_D^{24} 1·4570, $[\alpha]_D^{20}$ −12·7° (*c* 2·4 in chloroform) (Found: C, 59·5; H, 8·1. $C_{15}H_{24}O_6$ requires C, 60·0; H, 8·1%).

Addition of Ethanolamine to* 1,2:5,6-*Di*-O-*isopropylidene*-D-*glucofuranose* 3-*Crotonate.—To the ester (3·691 g.) in ether (75 ml.) was added ethanolamine (0·675 ml.). The whole was kept at room temperature for 70 hr., then concentrated under reduced pressure to a syrup (4·458 g., 102%), that in a short-path still volatilised at 140°/0·005 mm. It was **1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose*** (**β-2′-*hydroxyethylaminobutyrate***) (VIII) (Found: C, 55·5; H, 8·3; N, 3·0. $C_{18}H_{31}NO_8$ requires C, 55·6; H, 8·1; N, 3·6%).

This ester (0·397 g.) was kept in pyridine (10 ml.) with toluene-*p*-sulphonyl chloride (0·43 g.) at room temperature for 22 hr., then poured into ice-water and treated in the usual manner to give, as a syrup, **1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose* 3-(β-2′-*toluene*-p-*sulphonyloxyethylaminobutyrate*) *toluene*-p-*sulphonate*** (Found: C, 53·6; H, 6·3; S, 8·8. $C_{32}H_{45}NO_{13}S_2$ requires C, 53·7; H, 6·3; S, 9·0%).

The ester (VIII) (0·717 g.) slowly crystallised. Extraction with hot light petroleum (b. p. 60—80°) then left a residue (0·251 g., 92%), which after recrystallisation from acetone–alcohol had m. p. 178—180°, undepressed upon admixture with β-2′-hydroxyethylaminobutyric acid (V). Concentration of the light petroleum liquors afforded di-*O*-isopropylidene-D-glucose, m. p. 111—112°, in theoretical yield. This hydrolysis was accelerated by addition of water.

Addition of Ethylenediamine to* 1,2:5,6-*Di*-O-*isopropylidene*-D-*glucofuranose* 3-*Crotonate.—A solution of the crotonate (3·155 g.) and ethylenediamine (0·32 ml.) in ethanol (75 ml.) was kept at room temperature for 2¾ days before being concentrated under reduced pressure to a straw-coloured syrup (3·802 g., 102%). A sample (0·860 g.) was distilled to give fractions (*a*) (0·390 g.), b. p. 110—120°/0·01 mm. (bath-temp.), m. p. 105° (impure di-*O*-isopropylidene-D-glucose), and (*b*) (0·258 g.), b. p. 155—170°/0·01 mm. (bath-temp.), n_D^{20} 1·4680. The latter was ***bis*-(1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose*) 3,3′-[NN′-*ethylenedi*-(β-*aminobutyrate*)]** (XV) and underwent autohydrolysis on storage (Found: 56·9; H, 8·1; N, 3·0. $C_{34}H_{56}N_2O_{14}$ requires C, 57·0; H, 7·9; N, 3·9%).

The ester (2·939 g.) and water (50 ml.) were heated together for 3 hr. at 75—80°, and the resulting solution concentrated under reduced pressure to give a partly crystalline syrup (2·814 g.). This was extracted with light petroleum (4 × 50 ml.; b. p. 60—80°), concentration of the extracts giving di-*O*-isopropylidene-D-glucose (1·372 g., 72%). The residue was further extracted with acetone (50 ml.), concentration of the extract giving a syrup (0·659 g., 24%) which crystallised to give more di-*O*-isopropylidene-D-glucose, m. p. 105—108·5°. The hygroscopic residue was digested with hot ethanol, affording the crystalline acid (IV) (0·180 g., 21%) which after two recrystallisations from water–ethanol–acetone had m. p. 217·5—218·5° (Found: C, 51·5; H, 8·4; N, 11·7. Calc. for $C_{10}H_{20}N_2O_4$: C, 51·8; H, 8·6; N, 12·1%).

Addition of* 6-*Amino*-6-*deoxy*-1,2-O-*isopropylidene*-D-*glucofuranose to* 1,2:5,6-*Di*-O-*isopropylidene*-D-*glucofuranose* 3-*Crotonate.—A solution of the amino-sugar (0·137 g.) and the crotonate (0·206 g.) in ethanol (10 ml.) was kept at room temperature for 8½ days, the optical rotation falling from $[\alpha]_D$ −28·5° to −18·1°. The solution was concentrated to a syrup, and ether was added, giving an amorphous unidentified product (0·130 g.). Concentration of the mother-liquors gave a syrup (0·269 g.) which in a short-path still at 170°/0·005 mm. gave the ***amino*-*ester*** (XIII) (Found: C, 54·5; H, 7·6; N, 2·3. $C_{25}H_{41}NO_{12}$ requires C, 54·9; H, 7·6; N, 2·6%).

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The syrup partly crystallised during several months and was then extracted with hot light petroleum (b. p. 60—80°) to give impure di-*O*-isopropylidene-D-glucose, m. p. 100—102°.

The crude syrup (XIII) (5·586 g.) was stirred for 5 hr. at room temperature with water (80 ml.); crystals (1·926 g.) that separated recrystallised from ethanol, giving di-*O*-isopropylidene-D-glucose 3-crotonate, m. p. 66—67·5°. Concentration of the aqueous solution gave a syrup (3·660 g.) which was extracted with hot light petroleum (b. p. 40—60°). The residue (3·413 g.) crystallised from ethanol–ether to give material (0·623 g.) of m. p. 208—209·5°; several recrystallisations of this afforded 6-(2-*carboxy*-1-*methylethylamino*)-6-*deoxy*-1,2-O-*isopropylidene*-D-*glucofuranose* (XIV), m. p. 187—189° (C, 51·0; H, 7·7; N, 4·2. $C_{13}H_{23}NO_7$ requires C, 51·2; H, 7·6; N, 4·6%).

Addition of 3-O-2′-*Aminoethyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose to* 1,2:5,6-*Di*-O-*isopropylidene*-D-*glucofuranose* 3-*Crotonate*.—A solution of the amine (0·387 g.) and the ester (0·420 g.) in ethanol (25 ml.) was kept at room temperature for 18 hr. before being concentrated to a syrup. Distillation of the residue gave fractions (*a*) b. p. 140°/0·005 (bath-temp.), n_D^{22} 1·4689, which slowly crystallised to give 1,2:5,6-di-*O*-isopropylidene-D-glucose 3-crotonate, m. p. 55—56°, and (*b*) b. p. 175°/0·005 mm., n_D^{23} 1·4680. The latter was the *ether-ester* (X) (0·253 g.) (Found: C, 57·2; H, 7·7; N, 1·9. $C_{30}H_{49}NO_{13}$ requires C, 57·1; H, 7·8; N, 2·2%). This (0·097 g.) was digested with hot water for 1 hr., and the resulting solution concentrated to a syrup (0·052 g.), that distilled (short-path) at 120°/0·01 mm. The volatile residue (0·045 g.) partly crystallised (0·012 g.) on trituration with ether. Concentration of the ethereal mother-liquors gave a syrup which sublimed at 100°/15 mm. to give white needles, m. p. 100—104°, of di-*O*-isopropylidene-D-glucose.

Addition of 6-O-2′-*Aminoethyl*-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose to* 1,2:5,6-*Di*-O-*isopropylidene*-D-*glucofuranose* 3-*Crotonate*.—A solution of the amine (0·853 g.) and the crotonate (0·919 g.) in ethanol (50 ml.) was kept at room temperature for 18 hr. before being concentrated at 40° to a syrup. Fractional distillation of the syrup gave fractions (*a*) (0·464 g.), b. p. 130—140°/0·005 mm. (bath-temp.) (Found: C, 56·7; H, 7·7%), (*b*) (0·418 g.), b. p. 135—150°/0·005 mm. (bath-temp.) (Found: C, 57·7; H, 7·9%), and (*c*) (0·296 g.), b. p. 175—190°/0·005 mm. (bath-temp.), n_D^{23} 1·4700, $[\alpha]_D^{20}$ −68·6° (*c* 0·79 in chloroform). The last was the 1,2:5,6-*di*-O-*isopropylidene*-D-*glucose* 3-*ester* of the galactose derivative (XVIII) (Found: C, 56·9; H, 7·8; N, 2·3. $C_{30}H_{49}NO_{13}$ requires C, 57·1; H, 7·8; N, 2·2%).

This addition compound (0·825 g.) was suspended in water (50 ml.) at room temperature for 4 days. The insoluble residue (0·211 g.) was unhydrolysed compound. Concentration of the aqueous solution gave a syrup (0·548 g.) which was extracted with light petroleum (3 × 20 ml.; b. p. 60—80°). The residue (0·077 g.) was crystallised several times from ethanol–ether–light petroleum (b. p. 40—60°) to give 6-O-[2-N-(2-*carboxy*-1-*methylethyl*)*aminoethyl*]-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose* (XVIII), m. p. 156—157·5°, $\nu_{max.}$ 1600 cm.$^{-1}$ (ionised amino-acid) (Found: N, 3·9; $C_{18}H_{31}NO_8$ requires N, 3·6%).

Addition of 3-O-3′-*Aminopropyl*-1,2:5,6-*di*-O-*isopropylidene*-D-*glucofuranose to* 1,2:5,6-*Di*-O-*isopropylidene*-D-*glucofuranose* 3-*Crotonate*.—A solution of the amine (2·990 g.) and the crotonate (3·10 g.) in ethanol (200 ml.) was kept at room temperature for 2 days and then concentrated at 40°. The syrup (2·087 g.) was distilled to give fractions (*a*) b. p. 135°/0·005 mm. (bath-temp.) (which crystallised to give di-*O*-isopropylidene-D-glucose, m. p. and mixed m. p. 111·5—113°), (*b*) b. p. 160—165°/0·005 mm., n_D^{18} 1·4677, $[\alpha]_D$ −35·0° (*c* 2 in chloroform) (Found: C, 57·9; H, 8·1; N, 1·1%), and (*c*) (0·477 g.) b. p. 165°/0·005 mm. (bath-temp.), n_D^{18} 1·4670, $[\alpha]_D$ −21·2° (*c* 2 in chloroform). The last was the 3-*ester* of 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose and 3-*O*-[3-*N*-(2-carboxy-1-methylethyl)aminopropyl]-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (Found: C, 57·9; H, 8·3; N, 2·1. $C_{31}H_{51}NO_{13}$ requires C, 57·7; H, 8·0; N, 2·2%).

Autohydrolysis of an aqueous suspension of the addition product gave a syrup from which only di-*O*-isopropylidene-D-glucose was isolated.

Addition of 6-O-3′-*Aminopropyl*-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose to* 1,2:5,6-*Di*-O-*isopropylidene*-D-*glucofuranose* 3-*Crotonate*.—A solution of the amine (4·996 g.) and the crotonate (5·106 g.) in ethanol (200 ml.) was kept at room temperature for 18 hr. and then concentrated at 40° to a syrup, n_D^{23} 1·4650, $[\alpha]_D^{23}$ −57·4° (*c* 1·0 in chloroform). A sample was distilled to give 1,2:5,6-*di*-O-*isopropylidene*-D-*glucose* 3-*ester*, n_D^{23} 1·4670, $[\alpha]_D^{23}$ −60·8° (*c* 1·0 in chloroform), b. p. 135°/0·005 mm. (bath-temp.), of the acid (XIX) (Found: C, 57·3; H, 7·7; N, 1·9. $C_{31}H_{51}NO_{13}$ requires C, 57·7; H, 8·0; N, 2·2%).

The undistilled reaction product (3·664 g.) was triturated with water (15 ml.) and then kept

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at room temperature for 3 days. The aqueous layer was decanted from the residue (0·870 g.) and concentrated under reduced pressure to a syrup (2·440 g.) which was extracted with light petroleum (b. p. 60—80°) to leave material (0·995 g.), m. p. 176·5—178°. Several recrystallisations from light petroleum (b. p. 60—80°) gave the 6-O-[3-N-(2-*carboxy*-1-*methylethyl*)*amino*-*propyl*]-1,2:3,4-*di*-O-*isopropylidene*-D-*galactopyranose* (XIX), m. p. 190—191·5°, $[\alpha]_D^{23}$ −64·0° (*c* 1·0 in chloroform) (Found: C, 56·4; H, 8·1; N, 3·6. $C_{19}H_{33}NO_8$ requires C, 56·5; H, 8·3; N, 3·5%). The petroleum extract gave di-*O*-isopropylidene-D-glucose (1·390 g.), m. p. 111—112°.

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British Rayon Research Association, Heald Green Laboratories, Wythenshawe, Manchester, 22.
[Present addresses: (W. M. C.) Imperial Chemical Industries Ltd., Fibres Division, Harrogate, Yorks.
(J. E. M.) Svenska Träforskningsinstitutet, Stockholm, Sweden.] [*Received, January 26th*, 1961.]

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564. *Sulphates of Monosaccharides and Derivatives. Part III.*[1] *Acid Hydrolysis.*

By M. J. Clancy and J. R. Turvey.

The hydrolysis of the glycosidic linkages in various glycoside sulphates at 65° in 1·5N-hydrochloric acid has been compared with that in the parent glycosides. The results show that the presence of a sulphate group in a glycoside stabilises the glycosidic linkage to acid, the effect being greater for a 6-sulphate than for a 3-sulphate. The acidic fragmentation of polysaccharide sulphates is discussed in the light of these findings.

Linkage analysis of a polysaccharide by partial acid hydrolysis [2] depends on the production of oligosaccharide fragments, but the constitution of these depends on the relative stabilities to acid hydrolysis of the glycosidic linkages in the polysaccharide. Factors governing this stability include the sugar involved, and the type and configuration of the glycosidic linkage.[3] In polysaccharide sulphates the presence of the sulphate group, which is itself acid-labile, may also influence the rate of hydrolysis of glycosidic linkages, but little is known regarding the magnitude of any such effects. The acid hydrolysis of some methyl glycoside sulphates has now been studied and compared with the hydrolysis of the parent glycosides and of the free sugar sulphates.

Hydrolysis of glycosidic linkages was followed by determination of the reducing power, and the liberation of sulphate by an alkalimetric method. For obvious reasons, it was impracticable to use sulphuric acid for the hydrolyses and hydrochloric acid at 1·5N-concentration was used throughout, corrections being made for loss of sugar due to degradation. Since the hydrolysis of a methyl glycoside sulphate to the free sugar, methanol, and sulphate is the result of two concurrent reaction sequences, a kinetic analysis of the results is difficult. For such an analysis, only the initial rates should be considered (*i.e.*, before the intermediate products have reached significant concentrations) but we are interested in partial hydrolysis studies, which involve a late stage in the overall reaction. The overall reaction is approximately of the first order since the graphical plot of log concentration against time is almost linear. Comparison may therefore be made between the apparent rate coefficients obtained from such a plot and the true rate coefficients for the hydrolysis of a glycoside or of a sugar sulphate. However, the results given in the Table for the methyl glycoside sulphates cannot be regarded as more than a semiquantitative guide to differences in reaction rates.

[1] Part II, *J.*, 1961, 1692.
[2] Peat, Whelan, and Edwards, *J.*, 1955, 358.
[3] Whistler and Smart, "Polysaccharide Chemistry," Academic Press Inc., New York, 1953, p. 54.

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A study of the hydrolysis of methyl β-D-galactopyranoside 6-sulphate at various temperatures showed that at 35° no appreciable hydrolysis occurred; at 65° both glycosidic and ester linkages were hydrolysed at a convenient rate for study, and at 100° the rates were considerably accelerated. Between 65° and 100°, the increase in the rate of glycoside hydrolysis was approximately the same as that of ester hydrolysis, indicating that changes in reaction temperature do not appreciably alter the relative rates of hydrolysis of the two

Acid Hydrolysis of Glycose and Glycoside Monosulphates.

Compounds	Reaction temp.	Rate coefficients × 10^5 (sec.$^{-1}$) Ester hydrolysis	Glycoside hydrolysis
Methyl β-D-galactopyranoside 6-sulphate * ...	65°	2·21	1·68
	100	39·1	27·9
Methyl β-D-galactopyranoside	65	—	13·04
D-Galactose 6-sulphate	65	1·86	—
	100	33·2	—
Methyl α-D-glucopyranoside 3-sulphate * ...	65	4·38	0·64
Methyl α-D-glucopyranoside	65	—	1·82
Methyl β-D-glucopyranoside 3-sulphate * ...	65	1·92	1·43
Methyl β-D-glucopyranoside	65	—	4·09
D-Glucose 3-sulphate	65	5·91	—

* Apparent rate coefficients (see text).

linkages (see Table). A more interesting effect is shown by a comparison of the glycoside hydrolysis in a glycoside sulphate with that in the parent glycoside. Thus the rate of hydrolysis of methyl β-D-galactopyranoside is several times faster than that for methyl β-D-galactopyranoside 6-sulphate; for methyl α- and β-D-glucopyranosides the rates are appreciably faster than for their 3-sulphates, but the effect is less pronounced than that shown by the galactoside 6-sulphate. It is apparent, therefore, that a sulphate group stabilises the glycosidic linkage and that a 6-sulphate shows a greater stabilising effect than a 3-sulphate.

The reason for this stabilising effect is not clear but a possible explanation can be given. Recent work [4] has shown that the rate-determining step in the acid-catalysed hydrolysis of glycosides probably involves the formation at position 1 of a carbonium ion from the conjugate acid of the glycoside. This stage probably involves a change in conformation from a chair to a half-chair form [5] and it has been suggested that, during this stage, bulky substituents in equatorial positions increase the non-bonded interactions or repulsions and, as a consequence, increase the stability of these glycosides to acid hydrolysis. Both a 3-sulphate on glucose and a 6-sulphate on galactose occupy equatorial positions in the C1 conformation of these sugars and therefore come within this category.

A further point of interest in this study was the effect of a glycosidic linkage on the rate of hydrolysis of the sulphate group (Table). For methyl α-D-glucopyranoside-3-sulphate compared with glucose 3-sulphate, and for the galactoside 6-sulphate compared with galactose 6-sulphate, the effect was very small. Only in the case of methyl β-D-glucopyranoside 3-sulphate did the presence of a glycosidic linkage decrease appreciably the rate of hydrolysis of the sulphate group. The reason for this is not clear.

In view of the reported racemisation of optically active s-butyl hydrogen sulphate when treated with acid,[6] both of the methyl glucoside sulphates and D-glucose 3-sulphate were completely hydrolysed and the products examined. The only sugar product detected in each case was glucose. From galactose 6-sulphate and the galactoside 6-sulphate only galactose is expected and this was verified.

From these results it is concluded that it should be possible to isolate mono- and oligosaccharide sulphates from partial acid-hydrolysates of sulphated polysaccharides. The

[4] Banks, Meinwald, Rhind-Tutt, Shaft, and Vernon, *J.*, in the press.
[5] Foster and Overend, *Chem. and Ind.*, 1955, 566; Edward *ibid.*, 1955, 1102.
[6] Burwell, *J. Amer. Chem. Soc.*, 1945, **67**, 220.

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recent isolation of galactose 6-sulphate from one seaweed mucilage [7] and the production of oligosaccharide sulphates from another [8] support this view. It is further suggested that, during the early stages of hydrolysis of a sulphated polysaccharide, there would be a tendency for oligosaccharides with sulphate on sugar units other than the reducing-end unit to accumulate.

Experimental

Preparative and Analytical Techniques.—These were as previously described.[1]

Methyl α-D-*glucopyranoside* 3-(*ammonium sulphate*), having $[\alpha]_D^{18}$ +78·6° (*c* 2, in H_2O) and m. p. 165—166° (decomp.) (Found: S, 11·7. $C_7H_{17}NO_9S$ requires S, 11·1%), was isolated from the products obtained by sulphation of methyl α-D-glucoside. When it (0·15 g.) was oxidised in 4—5 molar excess of 46mM-periodate at room temperature the following results were obtained:

Time (hr.)	0·33	0·66	1·00	19
Periodate consumed (mol.)	0·00	0·08	0·17	0·22
Formic acid liberated (mol.)	0·05	0·07	0·08	0·13

These results are consistent with a methyl glucopyranoside 3-sulphate.

Methyl β-D-*glucopyranoside* 3-(*ammonium sulphate*), similarly isolated, had $[\alpha]_D^{16}$ −13·3° (*c* 1 in H_2O) and m. p. 155° (decomp.) (Found: S, 11·3%). Periodate oxidation, carried out as above, gave the following results:

Time (hr.)	1·0	5·0	24	48
Periodate consumed (mol.)	0·0	0·0	0·0	0·0
Formic acid liberated (mol.)	0·0	0·0	—	—

These results are in excellent agreement with expectation for methyl β-D-glucopyranoside 3-(ammonium sulphate).

Acid Hydrolysis.—Samples (1 mmole) of various glycoses, glycose monosulphates, glycosides, and glycoside monosulphates were dissolved in 1·5N-hydrochloric acid (100 ml.), previously heated to the temperature of the experiment, and kept at the selected temperature. Serial samples (*ca.* 5 ml.) were withdrawn, quickly cooled in ice-water to stop hydrolysis, and then allowed to equilibrate to room temperature.

The free sulphate was determined by mixing a portion (1 ml.) of the cooled reaction mixture in a Pyrex centrifuge tube (10 ml. capacity) with benzidine reagent [9] (5 ml.). After being kept for 5 min. at room temperature, the tube was immersed in ice-water for 10 min. and then centrifuged at 3000 r.p.m. for 5 min. The supernatant liquid was carefully decanted and the precipitate washed twice with 95% (v/v) aqueous ethanol (5 ml.) and centrifuged as above. To the precipitate was then added hot carbonate-free distilled water (2—2·5 ml.) and Phenol Red solution (0·01% in water; 0·1 ml.), and the tube was placed in a boiling-water bath. After a few minutes most of the precipitate usually dissolved. The tube was then removed from the bath, and a fine Pyrex jet was introduced into the tube for the delivery of carbon dioxide-free air to stir the mixture, which was titrated against 2mM-sodium hydroxide until the yellow colour of the indicator underwent the first change of colour. The tube was then placed in the boiling-water bath for 0·5—1 min. to ensure complete dissolution of the benzidine sulphate. The titration was continued if the yellow colour returned. For each determination duplicate readings were taken and each reading was corrected by subtracting a blank value obtained by titrating indicator and carbonate-free distilled water in the same way. The inorganic sulphate in terms of moles of sulphate per 100 ml. was derived by multiplying the titre figure by 10^{-4}. Control experiments had shown that the recovery of sulphate by this procedure varied from 98 to 103%.

The reducing power was determined on a portion (1—2 ml.) of the cooled reaction mixture by the Somogyi titrimetric method,[10] a correction being made for the loss of reducing power through destruction of sugar by hydrochloric acid.

[7] Turvey and Rees, *Nature*, 1961, **189**, 831.
[8] Painter, *Chem. and Ind.*, 1959, 1488.
[9] "The B.D.H. Book of Organic Reagents for Analytical Use," The British Drug Houses Ltd., London, 8th edn., p. 16.
[10] Somogyi, *J. Biol. Chem.*, 1945, **160**, 61.

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Complete Acid Hydrolysis of Glycose and Glycoside Monosulphates.—Quantities of the sugar sulphates were separately hydrolysed in 1·5N-hydrochloric acid for 5 hr. The hydrolysates were then cooled, neutralised with silver carbonate, and filtered and the soluble silver was removed with hydrogen sulphide. The solutions were again filtered and the clear filtrates separately concentrated under reduced pressure. Samples of the residues were examined by partition chromatography on paper and by ionophoresis. The only sugar detected in each case was the parent sugar.

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DEPARTMENT OF CHEMISTRY, UNIVERSITY COLLEGE OF NORTH WALES,
BANGOR, CAERN. [*Received, November 7th*, 1960.]

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565. *The Transmission of Polar Effects through Aromatic Systems. Part II.*[1] *The Nitration of Benzyl Derivatives.*

By J. R. KNOWLES and R. O. C. NORMAN.

The partial rate factors for nitration, by nitric acid in acetic anhydride, of toluene, benzyl methyl ether, chloride, and cyanide, ethyl phenylacetate, and phenylnitromethane have been measured. They are discussed with reference to the original Baker–Nathan theory of hyperconjugation and to more recent theories. It is concluded that time-variable release of electrons from methylene groups bonded to the benzene nucleus is important in determining rates of substitution at that nucleus. It is found also that the ability of a group $-CH_2X$ to release electrons in this way falls off as the electron-attracting capacity of X increases. The relation between the observed rates of nitration and the electron-attracting power of X (measured by Taft's σ_I-parameter) is discussed.

SINCE the original proposal by Baker and Nathan [2] in 1935 that alkyl groups bonded to unsaturated systems can release electrons by a conjugative mechanism, several theories have been advanced to explain the behaviour of these groups in such environments. Burawoy and Spinner [3] postulated that the Baker–Nathan order of electron-release by alkyl groups results from steric hindrance to bond contraction in electron-deficient transition states. They suggested that in the solvolysis of an alkyl halide $R{\cdot}CH_2X$ the contraction and stabilisation of the $R{-}CH_2^+$ bond (in the transition state which precedes the carbonium ion) will be reduced by steric repulsions increasing with the size of R, making methyl more reactive than t-butyl. Price and his co-workers [4] suggested that introduction of a bulky alkyl group *meta* or *para* to the reaction centre in aromatic side-chain reactions would to some extent prevent the solvent dipoles from stabilising the charge on the molecule in the transition state, decreasing the solvation energy and effectively increasing the activation energy. This "bulk" effect explained the hydrolysis rates of *m*- and *p*-alkylbenzoic esters, and the similarity between the relative rates of the bromination in the PhR and $Ph{\cdot}CH_2R$ series, which are both [5] $Me > Et > Pr^i > Bu^t$, whereas this order for the $Ph{\cdot}CH_2R$ series does not follow from the Baker–Nathan postulate. Schubert *et al.*[6] extended Price's ideas, and said that the *inherent* order of

[1] Part I, *J.*, 1961, 2221.
[2] Baker and Nathan, *J.*, 1935, 1844.
[3] Burawoy and Spinner, *J.*, 1954, 3752.
[4] Price and Lincoln, *J. Amer. Chem. Soc.*, 1951, **73**, 5836; Price and Belanger, *ibid.*, 1954, **76**, 2682.
[5] Berliner and Berliner, *J. Amer. Chem. Soc.*, 1949, **71**, 1195.
[6] Schubert, Craven, Minton, and Murphy, *Tetrahedron*, 1959, **5**, 194; Schubert and Sweeney, *J. Org. Chem.*, 1956, **21**, 119.

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electron-release from alkyl groups is the inductive one, but that for experiments in polar solvents (where the Baker–Nathan order may obtain) we are seeing, not an inversion of the inherent inductive order, but an indirect effect of steric hindrance to solvation of electron-deficient sites near the alkyl group.

Schubert's theory has been of much value in the re-interpretation of many solvolytic reactions and aromatic substitutions where the electronic effects of alkyl groups are important. His theory is relevant to the comparison of the behaviour of one alkyl group with that of another, but it was not clear whether it could take account of the behaviour of an alkyl *residue*, for instance, the methylene group in benzyl compounds.

The known values of the partial rate factors of benzyl chloride in nitration [7] cannot be reconciled with an extension of the theory of Schubert *et al.* to alkyl residues. The *meta*-position of this molecule is deactivated, which indicates that the chloromethyl group is electron-withdrawing relative to hydrogen. Now, in the transition state for electrophilic substitution at the *para*-position, $C_{(1)}$ of the benzene nucleus bears a partial positive charge (cf. I), and so, because of the $-I$ effect of the chloromethyl group, the *para*-position should be more deactivated than the *meta*-position in the transition state for which there is less positive charge on $C_{(1)}$ (II). Moreover, both the theory of Burawoy and Spinner (the $-CH_2X$ group being bulkier than hydrogen), and the theory of Schubert *et al.* (the $-CH_2X$ group restricting solvation more than hydrogen), predict that benzyl compounds will be less reactive at the *ortho*- and *para*-positions than at the *meta*-positions. This is contrary to the facts for benzyl chloride, for which the *meta* : *para* ratio in nitration is about 1 : 3.

We therefore surveyed the nitration of benzyl systems quantitatively, in an attempt to elucidate the electronic characteristics of the methylene residue. Nitration was chosen because some information was already available about the nitration of benzyl compounds, because of the convenient rates of reaction, and because of the stability and relative ease of isolation of the nitrobenzyl isomers. The partial rate factors in nitration for a representative series of benzyl systems have now been determined, and are set out in Table 1.

TABLE 1. *Partial rate factors in nitration (acetyl nitrate at 25°).*

Compound	*ortho*	*meta*	*para*	Compound	*ortho*	*meta*	*para*
PhMe	42·4	1·89	62·6	$Ph{\cdot}CH_2Cl$	0·716	0·296	2·24
$Ph{\cdot}CH_2{\cdot}CO_2Et$	6·29	1·52	7·55	$Ph{\cdot}CH_2{\cdot}CN$	0·252	0·208	1·15
$Ph{\cdot}CH_2{\cdot}OMe$	9·97	1·32	16·3	$Ph{\cdot}CH_2{\cdot}NO_2$	0·0822	0·200	0·167

In some cases our results differ from those obtained by previous workers. Only for benzyl chloride,[7] ethyl phenylacetate,[7] and phenylnitromethane [8] had quantitative studies of nitration previously been made, product analyses being by "classical" chemical methods. We checked the overall reactivities in nitration of benzyl chloride and ethyl phenylacetate by competitive experiments between them and between (i) ethyl phenylacetate and t-butylbenzene, (ii) t-butylbenzene and toluene, and (iii) toluene and benzene. From these comparisons, overall reactivities with respect to benzene were calculated. Our value of 25·2 for the overall reactivity of toluene in nitration at 25° falls between the two known values of 27 and 23 for this reaction at 0° and 30° respectively.[9] The overall reactivity of ethyl phenylacetate obtained by us (3·86) agrees tolerably with that obtained

[7] Ingold and Shaw, *J.*, 1949, 575.
[8] Baker, *J.*, 1929, 2257.
[9] Ingold, Lapworth, Rothstein, and Ward, *J.*, 1931, 1959.

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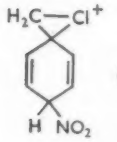
by Ingold and Shaw [7] (3·66), but we found a higher value (0·711) for benzyl chloride than they did (0·302). Baker [8] determined approximate isomer ratios for the nitration of phenylnitromethane: we have obtained accurate values, using infrared spectrophotometry for analysis of the isomer mixture. Generally, we have more confidence in our results since our analytical methods are more direct physical techniques.


(III)

The partial rate factors for nitration of benzyl chloride confirm the *ortho-para*-orientation reported previously. This could be explained in terms of a neighbouring-group effect, involving participation of chlorine in a three-membered ring, structures such as (III) being contributors to the transition state in an electrophilic substitution. This type of interaction has been well established for allylic systems.[10,11] The criterion for *ortho-para*-activation in a benzyl system would then be the existence in the side-chain of an atom with unshared electrons in a sterically favourable position for neighbouring-group interaction. We tested this hypothesis in three ways.

First, in benzyl cyanide, the only atom with unshared electrons is nitrogen, but since the CN group is linear this unshared pair can never be in a favourable position for interaction with $C_{(1)}$ of the benzene nucleus. The isomer ratios obtained in the nitration of benzyl cyanide were not very different (*ortho*: 24·4; *meta*: 20·1; *para*: 55·5%) from those of benzyl chloride (*ortho*: 33·6; *meta*: 13·9; *para*: 52·5%). The differences are easily accounted for by the larger inductive effect of the CN group than of Cl (Taft's σ^*-values [12] being CN 1·30 and Cl 1·05). The isomer ratios would not have been so similar if structure (III) had been important in substitution of benzyl chloride and impossible in that of benzyl cyanide.

The second test involved nitration of benzyl methyl ether. This, like benzyl chloride, has an atom with unshared electrons favourably placed for interaction with $C_{(1)}$ of the benzene nucleus. Further, oxygen is known to participate better in neighbouring-group interactions than chlorine.[11] If, for *ortho*- and *para*-substitution, neighbouring-group structures were important, then for substitution at these positions there should be a larger negative entropy of activation than for substitution at the *meta*-position, where such interactions are irrelevant. The difference between the entropies of activation at the *meta*- and *para*-positions of this compound was obtained from measurements of the isomer distributions in nitration at three temperatures.[13] The value of $\Delta\Delta S^{\ddagger}_{(p-m)} \approx 0{\cdot}45$ e.u. was obtained. Noble and Wheland,[14] after a comparable investigation of the activation entropies in the nitration of ethyl benzoate, point out that differences in activation entropies of this order (*i.e.*, $<0{\cdot}5$ e.u.) cannot be considered significant because of the necessary extrapolation. Thus these measurements provided no confirmation of a neighbouring-group effect.

The third test depended on the fact that a chlorine isotope effect should be observed in the nitration of benzyl chloride if there were a neighbouring-group interaction. If we assume complete formation of the Cl–$C_{(1)}$ bond at the transition state [see (III)], and neglect $C_{(\alpha)}$–Cl stretching and the strain in the three-membered ring, a maximum theoretical isotope effect can be calculated. The $^{35}k/^{37}k$ rate ratio (calculated on the basis of the difference in zero point energies [15]) is 1·047, and this, for 90% reaction of benzyl chloride (85% of which results in the formation of the *ortho*- and *para*-isomers), corresponds to a maximum possible isotopic enrichment in the unchanged material of about 13%. If this value is high by about a factor of ten (because of the simplifications made in its derivation)

[10] de la Mare and Pritchard, *J.*, 1954, 3910; de la Mare and Salama, *J.*, 1956, 3337; de la Mare and Ballinger, *J.*, 1957, 1481; de la Mare, Naylor, and Williams, *Chem. and Ind.*, 1959, 1020.
[11] de la Mare and Pritchard, *J.*, 1954, 3990.
[12] Taft, in "Steric Effects in Organic Chemistry," ed. Newman, John Wiley and Sons, Inc., New York, 1956, p. 595.
[13] Kent and Norman, *J.*, 1959, 1724.
[14] Noble and Wheland, *J. Amer. Chem. Soc.*, 1958, **80**, 5397.
[15] Cf. Bell, "The Proton in Chemistry," Methuen and Co., London, 1959, p. 184.

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an isotope effect should still be measurable by the mass-spectrometric method employed, by which the $^{35}Cl : ^{37}Cl$ ratio was determined within $\pm 0{\cdot}14\%$. Samples of benzyl chloride remaining after 70%, 80%, and 90% nitration showed no detectable difference in this ratio when compared with an unchanged sample.

From these three pieces of evidence it is concluded that neighbouring-group effects, if they occur, are kinetically insignificant (at least in nitration).

The pattern of the partial rate factors obtained (see Table 1) depends basically on the inductive effect of the group CH_2X. We see gradations in the behaviour of these compounds as the $-I$ effect increases, from compounds ($Ph{\cdot}CH_2X$) in which both *meta*- and *para*-positions are activated (X = H, OMe, CO_2Et) to compounds in which the *meta*-position is deactivated but the *para*-position activated (X = Cl, CN), to a compound in which both the *meta*- and the *para*-position are deactivated ($X = NO_2$). One important feature is that both benzyl chloride and benzyl cyanide are deactivated at the *meta*-position but activated at the *para*-position. The deactivation of the *meta*-positions in these compounds indicates that the groups CH_2Cl and $CH_2{\cdot}CN$ are electron-withdrawing with respect to hydrogen. Yet the activation of the *ortho*- and *para*-positions cannot be explained by the $-I$ effect. Nor can the theories of Burawoy and Spinner and of Schubert *et al.* account for this activation; indeed, they predict the reverse, as is pointed out above.

We have therefore to invoke some polarisability effect for the CH_2Cl and $CH_2{\cdot}CN$ groups, and this, since it must involve time-variable electron-release from a methylene group, is what is understood as hyperconjugation.

On the basis of these arguments, the rate of substitution at the *meta*-position of a benzyl compound should be governed by the inductive effect of the CH_2X group. It has been found that the Hammett relation is obeyed for the substitution of many aromatic compounds at the *meta*-position.[16] Since few of the σ-values of the CH_2X groups are known, a direct Hammett plot (of the logarithm of the *meta*-partial rate factor against σ_m of the CH_2X group) cannot be realised. However, if there is a linear relation between Taft's σ_I-values for X,[17] and the σ_m-values for the CH_2X group, a linear graph of the Hammett type should be obtained. The results from this procedure are not very well fitted by a straight line, but the trend of decreasing f_m (where f_m is the *meta*-partial rate factor) with increasing inductive electron-withdrawal, is clear (Table 1). σ_I-Values derived by Taft [17] from different reaction series vary from 0·60 to 0·68, and from 0·50 to 0·58, for the NO_2 and the CN group respectively. Variations in σ_I of this order vitiate a more detailed analysis of our results in terms of Hammett constants. Another reason for the poor correlation is that the amount of *meta*-isomer obtained from the benzyl compounds is relatively small (usually less than 20%), and, since the range of *meta*-reactivities is only about one power of ten, $\log_{10} f_m$ is very sensitive to small errors in the isomer distribution.

For *para*-substitution in benzyl systems, both the inductive effect of the CH_2X group and the time-variable release due to the methylene residue are important. The graph of σ_I (for X in CH_2X) against $\log_{10} f_p$ is a curve (see the Figure) in which $\log_{10} f_p$ falls off increasingly rapidly as σ_I increases. Here the reactivities range over three powers of ten, and $\log_{10} f_p$ is less sensitive to small errors in the percentage of *para*-isomer. Our interpretation of the curve is as follows. Since the curve indicates that $\log_{10} f_p$ decreases more rapidly for a given change in σ_I at high values of σ_I, the contribution of hyperconjugation from the methylene group to the rate of reaction must itself fall off with increasing electron-demand by X. This is reasonable, since as the electron-pull of X in CH_2X increases, there will be a reduced concentration of electrons in the carbon–hydrogen bonds available for time-variable release.

Some experiments by Burton and Ingold [18] can also be best interpreted on this

[16] Roberts, Sanford, Sixma, Cerfontain, and Zagt, *J. Amer. Chem. Soc.*, 1954, **76**, 4525.
[17] Taft, *J. Phys. Chem.*, 1960, **64**, 1805.
[18] Burton and Ingold, *J.*, 1929, 2022.

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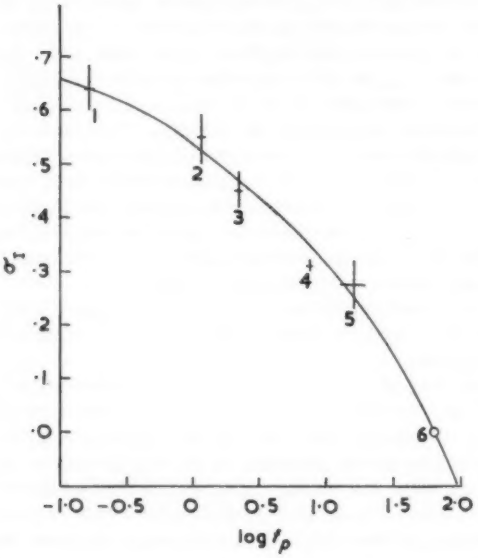
view, but it is opposite to a contention by Baker *et al.*[19] that hyperconjugative release *increases* when the electron-releasing system is attached to an electron-attracting group. The experiments of Baker *et al.* involved addition of bromine to various allylic compounds, and they obtained an order F > Cl > Br > CN for the reactivity of X in $X{\cdot}CH_2{\cdot}CH{=}CH_2$. It is very probable that, as is well established in other allylic systems, the order of reactivities which Baker *et al.* found is due, not to a decrease in hyperconjugative release,



Plot of log f_p *for* $Ph{\cdot}CH_2X$ *against* σ_I *for* X. X = : 1, NO_2; 2, CN; 3, Cl; 4, CO_2Et; 5, OMe; 6, H.

but to neighbouring-group effects. The degree of participation in neighbouring-group interactions is exactly in the order they found.

It is difficult, with the available data, to make any more specific or quantitative deductions about the electronic factors important in benzyl systems owing to the inaccuracy and variability of σ-values and the relatively small range of reactivities in benzyl compounds.

Experimental

Materials.—Ethyl phenylacetate, benzyl methyl ether, benzyl chloride, benzyl cyanide, t-butylbenzene, toluene, benzene, acetic anhydride, and bromoform were commercial materials, purified by distillation. "AnalaR" concentrated sulphuric acid and "AnalaR" fuming nitric acid (*d* 1·5) were used, a small quantity of urea being added to the latter before all nitrations. Phenylnitromethane was prepared by the method of Black and Babers [20] and was stored at −40° (m. p. −6° to −7°).

Analytical Methods.—Isomer ratios were determined by gas chromatography or infrared spectroscopy. For the gas chromatography, column conditions were those in which the three isomers were completely resolved. Standard mixtures of pure isomers were injected to confirm the proportionality between peak area and weight of isomer. The peak areas were calculated from the triangles formed by tangents to the Gaussian curve and the interpolated base-line. The isomers were extracted from the nitration mixture with ether four times. Standard mixtures of isomers were subjected to this procedure to check that no isomer was preferentially lost in the extraction.

For the infrared analyses, the region 9—13 μ was used, the experimental isomer concentrations being calculated from the spectra of near-replica synthetic mixtures of isomers, or

[19] Baker, Brieux, and Saunders, *J.*, 1956, 404.
[20] Black and Babers, *Org. Synth.*, 1943, Coll. Vol. II, p. 512.

by determining the extinction coefficients of each pure isomer at three different wavelengths and calculating the experimental isomer concentrations by solving the three simultaneous equations obtained. The method of calculation was checked by determining the concentration of synthetic mixtures containing known proportions of isomers. Carbon disulphide is not a good enough solvent for nitrobenzyl isomers; nitromethane absorbs increasingly between 11 and 13 μ; however, bromoform does not absorb seriously in the 9—13 μ region (only having a weak band at 870 cm.$^{-1}$) and dissolves at least 80 mg./ml. of the isomers. The purity of the bromoform is critical, since carbonyl bromide has a strong absorption band in the 750—800 cm.$^{-1}$ region. Bromoform was therefore redistilled (b. p. 40°/18 mm.) before each set of determinations. Depending on the extinction coefficients of the isomers concerned, 1 mm. or 0·1 mm. cells were used. Even with the 1 mm. cells, the weak absorption band of bromoform at 870 cm.$^{-1}$ was completely cancelled, the spectrometer retaining its response in this region. Conditions were always chosen to give peaks of between 30% and 70% absorption. The products were freed from unchanged starting material by distillation. The extraction procedure was in each case checked by means of synthetic mixtures. Spectroscopic determinations were made on a Perkin–Elmer self-recording infrared spectrophotometer, model 21A.

Overall reactivities were determined by competitive nitrations, the mixtures being analysed by gas chromatography. For most of the compounds, the relative decreases in the amounts of the reactants after the nitration were measured. To obtain the absolute differences in amount of material before and after nitration an internal standard was used. This was a compound entirely resistant to nitration under the conditions used * with a retention time different enough from those of the reacting compounds to give complete resolution. The ratios of the peak heights of each of the two compounds compared with that of the internal standard were obtained for the mixtures before and after nitration. In every case, changes in the ratios of peak heights were found to correspond to changes in the ratios of amounts of material to within 2%. Thus decreases in the values of (peak height of compound): (peak height of internal standard) were directly proportional to decreases in compound concentration. For all nitrations, a mixture of the two competing reactants and the internal standard was divided into two parts, which were placed in the thermostat bath. To one was added the nitrating mixture (nitric acid in acetic anhydride), and, to the other, acetic anhydride alone. After a suitable time, water was added to each part and the organic material extracted four times with ether. These mixtures were then injected alternately on to the gas-chromatographic column, and decreases in amount of each reactant determined. Between 60 and 100 injections of " pre "- and " post "-nitration mixtures from at least four competitive experiments were made in each comparison.

There are two limitations to this method of determining the overall reactivity. Reactivities cannot differ by a factor of more than about five, since the decreases in peak heights are too disparate for accurate determination of each; and compounds of widely differing boiling points (>100°) cannot be compared, since the retention times and peak shapes differ too much for easy or accurate analysis. The experimental ratio R, in which the compounds have undergone reaction, is equal to k_x/k_y, the true rate ratio, only in the limit of small amounts of reaction. At large amounts of reaction, the competing compounds will no longer be present in their initial ratio x_0/y_0. However, Ingold and Smith [22] deduced that, even for reasonable amounts of reaction, $k_x/k_y = \log(x/x_0)/\log(y/y_0)$, where x_0 and y_0 are the initial concentrations, and x and y are the final concentrations. This relation was used to calculate k_x/k_y in the present experiments.

The overall reactivity of toluene with respect to benzene was determined by *product* analysis, rather than by analysis of the amounts of starting material before and after nitration. Here again, the experimental ratio P, of formed products, is only equal to k_x/k_y in the limit of small amounts of reaction. The simplest procedure (which was adopted here) for obtaining k_x/k_y from product analysis is to nitrate 1 : 1 molar mixtures of reactants so that the total degree of nitration varies, say, from 5% to 50%. The value of P is plotted against the degree of nitration (which is known from the amount of acetyl nitrate added), and the line obtained extrapolated to zero reaction. This is the limit where $P = k_x/k_y$ and gives the latter ratio. Overall reactivities obtained in the various competitive reactions are set out in Table 2.

* It has already been shown that the straight-chain hydrocarbons (decane, undecane, and dodecane) do not react under the conditions used here.[21]

[21] Knowles, Norman, and Radda, *J.*, 1960, 4885.
[22] Ingold and Smith, *J.*, 1938, 905.

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Nitration of Ethyl Phenylacetate.—Pure samples of the three nitro-isomers were obtained by esterification of the corresponding acids,[23] by the Fischer–Speier method. Ethyl *o*-nitrophenylacetate had m. p. 65·5° (lit.,[24] 69°); ethyl *m*-nitrophenylacetate, m. p. 11—13°, b. p. 110°/0·1 mm. (Found: C, 57·05; H, 5·2; N, 7·15. Calc. for $C_{10}H_{11}NO_4$: C, 57·4; H, 5·3; N, 6·7%); ethyl *p*-nitrophenylacetate, m. p. 63·5—64° (lit.,[25] 64—66°).

The isomer ratio was determined by infrared spectroscopy. Extinction coefficients were

TABLE 2. *Overall reactivities from competitive experiments.*

Competing species A	Competing species B	Values of overall reactivity of A relative to B	Mean values	Calc. overall reactivities of A relative to benzene
$Ph{\cdot}CH_2CO_2Et$	$PhBu^t$	0·263		
		0·254	0·26	3·86
		0·264	(±2%)	
		0·254		
$PhBu^t$	PhMe	0·503		
		0·713		
		0·613	0·59	14·9
		0·523	(±14%)	
		0·700		
		0·490		
$Ph{\cdot}CH_2Cl$	$Ph{\cdot}CH_2{\cdot}CO_2Et$	0·189		
		0·188		
		0·184	0·184	0·711
		0·169	(±5%)	
		0·204		
		0·170		
$Ph{\cdot}CH_2{\cdot}OMe$	$Ph{\cdot}CH_2{\cdot}CO_2Et$	2·08		
		1·62		
		1·85	1·70	6·48
		1·37	(±15%)	
		1·46		
		2·08		
		1·46		
$Ph{\cdot}CH_2{\cdot}CN$	$Ph{\cdot}CH_2Cl$	0·506		
		0·463	0·486	0·345
		0·477	(±3%)	
		0·497		
$Ph{\cdot}CH_2{\cdot}NO_2$	$Ph{\cdot}CH_2Cl$	0·182		
		0·158		
		0·160	0·171	0·122
		0·172	(±6%)	
		0·165		
		0·188		
PhMe	C_6H_6	25·2		25·2

calculated for each isomer at 786 cm.$^{-1}$ (mainly *ortho*), 804 cm.$^{-1}$ (mainly *meta*), and 857 cm.$^{-1}$ (mainly *para* and *ortho*). From a synthetic mixture of isomers containing *o*- 44·44, *m*- 11·11, *p*- 44·44% by wt., percentages calculated from the spectrum were *o*- 43·8, *m*- 11·8, *p*- 44·4. A mixture of nitric acid (0·009 mole) in acetic anhydride (0·01 mole) was added dropwise to ethyl phenylacetate (0·01 mole) at 25° during 1 hr. The temperature variation was not more than 0·5°. After 12 hr. the mixture was transferred to a micro-fractional-distillation apparatus, and the system evacuated to 0·075 mm. After acetic anhydride (and any unchanged nitric acid) had distilled over, the temperature was raised slowly to 65°, to rid the mixture of any unchanged ethyl phenylacetate. The flask was cooled, the vacuum released at the flask (so that the incoming air could sweep over any ethyl phenylacetate vapour remaining), and the resulting isomer mixture analysed. To a 1 : 1 : 1 synthetic mixture of isomers were added some ethyl phenylacetate and acetic anhydride. This mixture was subjected to the treatment described above, and it was found that the isomer ratio was the same to within 1% after the distillation as before. Isomer ratios obtained from experimental nitrations were: *ortho* 54·3, *meta* 13·1, *para* 32·6 ± 0·5%.

The overall reactivity of ethyl phenylacetate with respect to benzene was obtained from the

[23] Norman and Radda, *J.*, in the press.
[24] Reissert and Scherk, *Ber.*, 1898, **31**, 395.
[25] Maxwell, *Ber.*, 1879, **12**, 1767.

following comparisons: (*a*) Ethyl phenylacetate and t-butylbenzene, with dodecane as the internal standard, were allowed to compete for an inadequate amount of acetyl nitrate for 3 hr. Column 1 (Table 3) was used for the anlysis, and the values for the relative reactivity are set out in Table 2.

TABLE 3. *Gas chromatographic columns.*

Columns used were packed with Apiezon " L " grease coated on Embacel (except columns 4 and 6, for which 50—80 mesh firebrick was the support). The bore of all columns was 4·5 mm.

Column no.	1	2	3	4	5	6	7	8	9
w/w % of stationary phase	20	20	20	20	20	30	30	20	10
Carrier gas	H_2	H_2	H_2	H_2	N_2 [a]	N_2 [a]	N_2 [a]	N_2 [a]	N_2 [a]
Flow rate (ml./min.)	69	67	64	40	34	72	55	24	32
Length of column (cm.)	100	100	100	200	400	50	200	400	100
Inlet pressure [b] of carrier gas (cm.)	61	61	48	49	65	34	46	65	43
Inlet heater temp. (approx.)	250°	250°	200°	250°	200°	130°	240°	240°	270°
Column temp.	178°	140°	154°	150°	145°	93°	156°	180°	148°

[a] Where nitrogen was used as the carrier gas, a hydrogen-inject flame-ionisation detector was used. In all other cases the eluting hydrogen stream was burned directly in such a detector. These detectors, coupled to a Sunvic recorder, gave a linear response. [b] Columns were run with atmospheric pressure at the outlet.

(*b*) t-Butylbenzene and toluene, with undecane as the internal standard. Column 2 (Table 3) was used.

(*c*) Toluene and benzene (for details, see below).

Nitration of Benzyl Methyl Ether.—*Methyl 2-nitrobenzyl ether* was obtained as a yellow liquid by refluxing 2-nitrobenzyl chloride (1 mole) with sodium (1 g.-atom) in methanol for 1 hr. The mixture was poured into water and extracted with ether, and the product was purified by chromatography on alumina. Fractional distillation (b. p. 64°/0·1 mm.) gave a pure product, which produced a single symmetrical peak on gas chromatography (Found: C, 57·7; H, 5·3; N, 8·9. $C_8H_9NO_3$ requires C, 57·5; H, 5·4; N, 8·4%). *Methyl 3-nitrobenzyl ether*, prepared by a similar procedure from 3-nitrobenzyl bromide, had b. p. 79°/0·1 mm. (Found: C, 56·7; H, 5·4; N, 8·8%). Methyl 4-nitrobenzyl ether formed yellow crystals, m. p. 26—27° (lit.,[26] 26—27°).

The isomer ratio was determined by gas chromatography. Column 8 (Table 3) was used, the isomers having the following retention times: *ortho* 25½, *meta* 35, *para* 37½ min. Isomer proportions obtained were *ortho* 51·3, *meta* 6·8, *para* 41·9 ± 0·4%.

Benzyl methyl ether was nitrated with a 1 : 1 mixture of nitric and sulphuric acid at 0°, 25°, and 50°, for the determination of the relative activation entropies. Column 8 of Table 3 was used for the analysis, the isomer ratios obtained being, at the above temperatures, *ortho* 27·3, 28·6, 30·9, *meta* 17·4, 18·1, 18·5, and *para* 55·3, 53·3, 50·6% respectively.

The overall reactivity of benzyl methyl ether was determined relative to that of ethyl phenylacetate. Dodecane was the internal standard, and column 4 (Table 3) was used for the analysis.

Nitration of Benzyl Chloride.—Pure samples of the three nitro-isomers were obtained by recrystallising commercial samples from methanol and light petroleum (b. p. 60—80°). 2-Nitrobenzyl chloride had m. p. 49° (lit.,[27] 48—49°); 3-nitrobenzyl chloride, m. p. 45° (lit.,[27] 45—47°); 4-nitrobenzyl chloride, m. p. 72° (lit.,[28] 71°).

The isomer ratio was determined by gas chromatography, column 9 (Table 3) being used. It was not possible to devise a column and conditions which would completely resolve 3- and 4-nitrobenzyl chloride. Resolution was adequate for reasonably reproducible isomer percentages, as follows: *ortho* 33·6, *meta* 13·9, *para* 52·5 ± 0·9%. The retention times of the isomers on the column used were: *ortho* 57½, *meta* 82½, *para* 91 min.

The overall reactivity of benzyl chloride was determined relative to that of ethyl phenylacetate. Dodecane was used as the internal standard and column 3 (Table 3) for the analysis.

Samples of benzyl chloride for the mass-spectrometric analysis were obtained as follows. Benzyl chloride was nitrated at 25° with 2 : 1 sulphuric–nitric acid. After 3 hr. water was added and the organic material extracted three times with ether. The ether extracts were

[26] Kleucker, *Ber.*, 1922, **55**, 1645.
[27] Gabriel and Bergmann, *Ber.*, 1883, **16**, 2059.
[28] Beilstein and Geitner, *Annalen*, 1866, **139**, 331.

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dried and evaporated. Benzyl chloride was obtained at 30°/0·1 mm. in a micro-fractional-distillation apparatus. Amounts of nitro-isomers and unchanged benzyl chloride were weighed to obtain the approximate percentage of nitration. The ^{37}Cl : ^{35}Cl ratio was determined for the following samples: before nitration 0·3206 ± 0·0008, after 70% nitration 0·3208 ± 0·0012, after 80% nitration 0·3208 ± 0·0022, after 90% nitration 0·3207 ± 0·0013. The values obtained do not indicate any change in the isotope ratio greater than experimental error.

Nitration of Benzyl Cyanide.—2-Nitrobenzyl cyanide [29] had m. p. 81·5—82·5° (lit., 82°). 3-Nitrobenzyl cyanide was prepared by refluxing a mixture of 3-nitrobenzyl bromide (1 mol.) in ethanol and potassium cyanide (1 mol.) in the minimum amount of water for 1 hr. After removal of the ethanol by distillation the organic material was extracted with ether and recrystallised from aqueous ethanol as yellow needles, m. p. 58·5—59·5° (lit.,[30] 61°). 4-Nitrobenzyl cyanide had m. p. 116° (from ethanol) (lit.,[31] 114—116°).

The isomer ratio was determined by infrared spectroscopy, the procedure being analogous to that employed for ethyl phenylacetate. Isomer ratios from experimental nitrations were calculated by spectrometric comparison with a synthetic 1 : 1 : 2 mixture of the 2-, 3-, and 4-isomers. The absorption at 786 (*ortho*), 922 (*meta* and *para*), and 831 cm.$^{-1}$ (*para*) was used. Isomer ratios obtained were: *ortho* 24·4, *meta* 20·1, *para* 55·5 ± 0·2%.

The overall reactivity was determined relative to that of benzyl chloride with decane as the internal standard. Column 5 (Table 3) was used for the analysis.

Nitration of Phenylnitromethane.—*o*-Nitrophenylnitromethane was prepared by refluxing 2-nitrobenzyl chloride (1 mol.) with sodium iodide (1 mol.) in acetone for 4 hr. The mixture was filtered while hot and the acetone distilled off. The residue of 2-nitrobenzyl iodide recrystallised from ethanol as green plates. It was dissolved in dry ether and treated with a 20% excess of silver nitrite. The mixture was stirred for 6 hr. at room temperature, then refluxed for 4 hr. The excess of silver salt was filtered off after cooling. Evaporation of the ether gave *o*-nitrophenylnitromethane as yellow plates [from ethanol, then light petroleum (b. p. 100—120°)], m. p. 67·5° (lit.,[32] 72°) (Found: C, 46·3; H, 3·25; N, 15·7. Calc. for $C_7H_6N_2O_4$: C, 46·2; H, 3·3; N, 15·4%). *m*-Nitrophenylnitromethane was prepared from a mixture of *m*-nitrobenzyl bromide and a 20% excess of silver nitrite in dry ether, which was stirred for 24 hr. at 0°, then 12 hr. at room temperature. The excess of silver salt was filtered off, and the ether solution concentrated until a solid separated, this product being isolated as above. The off-white needles of *m*-nitrophenylnitromethane had m. p. 95·5° (lit.,[32] 95—96°). *p*-Nitrophenylnitromethane [33] had m. p. 91° (lit.,[32] 90°).

The isomer ratio was determined by infrared spectroscopy by the method described above. Isomer ratios from experimental nitrations were calculated by comparison with synthetic 1 : 2 : 1 mixtures of the *ortho*-, *meta*-, and *para*-isomers. The absorption at 788 (*ortho*), 807 (*meta*), and 856 cm.$^{-1}$ (*para*) was used. Isomer ratios obtained were: *ortho* 22·5, *meta* 54·7; *para* 22·8 ± 0·5%.

The overall reactivity of phenylnitromethane was determined relative to that of benzyl chloride with undecane as the internal standard. A small quantity of dry ether was added to make a homogeneous mixture. Column 6 (Table 3) was used for the analysis.

Nitration of Toluene.—The isomer ratio was determined by gas chromatography of the nitration mixtures obtained from the competitive experiments (see below). Column 7 (Table 3) was used. Ratios obtained were: *ortho* 56·1, *meta* 2·5, *para* 41·4 ± 0·5%.

The overall reactivity of toluene with respect to benzene was measured by product analysis. Five mixtures. each containing 0·01 mole of toluene and 0·01 mole of benzene, were nitrated with acetyl nitrate. To these mixtures severally, 0·001, 0·002, 0·003, 0·006, and 0·01 mole of acetyl nitrate were added dropwise, and the flasks left in the thermostat bath for 48 hr., after which the reaction was virtually complete. From the peak areas of nitrobenzene and *p*-nitrotoluene (all three nitrotoluenes and nitrobenzene resolved under the conditions of column 7), the apparent partial rate factor at the *para*-position of toluene (f_p) was obtained. (This is the peak area of *p*-nitrotoluene divided by one-sixth of the peak area of nitrobenzene.) The values of apparent f_p were plotted against the amount of acetyl nitrate added, and the linear plot

[29] Rinderneckt, Koechlin, and Niemann, *J. Org. Chem.*, 1953, **18**, 971.
[30] Heller, *Annalen*, 1907, **358**, 349.
[31] Radziszewski, *Ber.*, 1870, **3**, 198.
[32] Holleman, *Rec. Trav. chim.*, 1896, **15**, 367.
[33] Kornblum, Smiley, Blackwood, and Iffland, *J. Amer. Chem. Soc.*, 1955, **77**, 6269.

obtained extrapolated to zero extent of reaction. The gradient of this line was less than one, so slight inaccuracies in the percentage of nitration, or in the values of apparent f_p, did not alter the intercept on the apparent f_p axis very much. The values obtained were:

Nitration (approx. %)	5	10	15	30	50
Apparent f_p (mean; ±2%)	61	58	54	47	38

The intercept at zero nitration is 62·6, which is the real f_p. From the isomer ratio obtained above, this gives an overall reactivity of 25·2 for toluene with respect to benzene in nitration with acetyl nitrate at 25°.

We are most grateful to Mr. H. J. M. Fitches of the Scientific Apparatus Engineering Department of Associated Electrical Industries Limited, for carrying out the mass-spectrometric analyses, and to Mr. A. E. Thompson for assistance with the gas-chromatographic apparatus. One of us (J. R. K.) thanks Merton College for a research scholarship.

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, December 29th*, 1960.]

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566. *The Association of n-Tetra-alkoxy- and n-Alkoxy-chloro-derivatives of Titanium.*

By R. L. MARTIN and G. WINTER.

The temperature and concentration-dependence of the molecular association of tetrabutoxytitanium(IV) has been measured in benzene solution by cryoscopic and calorimetric methods. Although the association follows a reaction of the third order it probably proceeds through an unstable dimer, $Ti_2(OBu)_8$. The energy of the intermolecular bonding between pairs of titanium atoms is 9·8 kcal. mole^{-1}. The chlorine derivatives $TiCl(OBu)_3$, $TiCl_2(OBu)_2$, and $TiCl_3$·OBu are trimeric, dimeric, and monomeric, respectively.

A structural hypothesis is postulated which differs from previous models in that a triangular rather than a linear arrangement of titanium atoms is envisaged.

A new and sensitive cryoscopic technique is described.

ALTHOUGH the tendency of n-alkyl titanates $Ti(OR)_4$ to associate is now well established,[1-5] the constitution of the resulting polymer remains open to speculation. It is generally believed [4-6] that association results from the ability of titanium to expand its co-ordination number when in an environment of donor atoms, but conclusive structural evidence is lacking to show whether quadrivalent titanium is five- or six-covalent in its alkoxides. No attempt has been made to measure directly the strength of the intermolecular bond which is believed to link pairs of metal atoms through alkoxide bridges as was first suggested

for thallium(I) methoxide in 1930 by Sidgwick and Sutton;[7] whether the bond is predominantly covalent (Ia) or electrostatic (Ib) is still unknown. While it is generally accepted that n-alkyl titanates associate to form trimers, the experimental evidence on

[1] Bradley, Mehrota, Swanwick, and Wardlaw, *J.*, 1953, 2025.
[2] Winter, *J. Oil Colour Chemists' Assoc.*, 1953, **36**, 689; M.Sc. Thesis, University of N.S.W., 1956.
[3] Bradley, Gaze, and Wardlaw, *J.*, 1957, 469.
[4] Coughlan, Smith, Katz, Hodgson, and Crowe, *J. Amer. Chem. Soc.*, 1951, **73**, 5652.
[5] Cullinane, Chard, Price, Millward, and Langlois, *J. Appl. Chem.*, 1951, **1**, 400.
[6] Bradley, *Nature*, 1958, **182**, 1211.
[7] Sidgwick and Sutton, *J.*, 1930, 1461.

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which this conclusion is based is sometimes in conflict, as may be seen from Table 1 which summarises some data from the literature.

In the present investigation, an attempt has been made to ascertain the energy of intermolecular bonding by measuring cryoscopically and calorimetrically the variation with concentration of the degree of association in benzene solution. The n-butoxide was selected as a typical ester of medium chain length, and mixed chloro- and butoxy-derivatives were also studied.

Association of Tetrabutoxytitanium(IV) *and its Chloro-derivatives in Benzene.*—The association of tetra-alkyl titanates has been investigated cryoscopically in benzene in the concentration range 0—0·03 (molar fraction of solute) by Coughlan *et al.*[4] For the compounds $Ti(OEt)_4$, $Ti(OPr)_4$, $Ti(OBu)_4$, and $TiCl(OEt)_3$, the degree of association increased from one to a maximum value of three in the concentration range 0—0·01. At higher concentrations, the association number was found to decrease with increasing concentration, a result which is incompatible with any reasonable scheme envisaged for an association equilibrium dependent on concentration and temperature alone.

The present data for three independent series of molecular-weight determinations for tetrabutoxytitanium in benzene over the range 0—15 $\times$ 10^{-2}m are shown in Fig. 1. The curve represents the increase in average molecular weight with mass of tetrabutoxytitanium added, and becomes asymptotic towards the molecular weight of the trimer

TABLE 1. *Molecular complexity of n-alkyl titanates* $Ti(OR)_4$.

Alkyl	Method	Solvent	Concn. (10^{-2} mol. fraction)	Complexity	Authors
Ethyl	Ebull.	Benzene	1·3—8·0	2·4	Bradley *et al.*[1]
Butyl	,,	Butanol	5·9	1·14	Winter [2]
			6·7	1·17	
			10·3	1·28	
			11·7	1·29	
			16·1	1·40	
			18·1	1·41	
Butyl	,,	,,	5·0	1·0	Bradley *et al.*[1, 3]
Pentyl	,,	Benzene	1·1—7·0	1·4	
Octyl	,,	,,	2·5—8·1	1·4	
Propyl	Cryosc.	,,	3·7	1·0	Coughlan *et al.*[4]
			8·9	2·4	
			13·3	3·0	
			17·8	2·9	
			21·7	2·8	
			28·3	2·7	
			36·1	2·5	
Butyl	,,	,,	6·0	2·01	Cullinane *et al.*[5]
			11·4	2·04	
			14·5	2·05	
Butyl	,,	,,	3·1	1·0	Coughlan *et al.*[4]
			5·0	1·3	
			8·3	3·0	
			12·2	3·0	
			22·0	2·8	
			23·0.	2·8	

(1020) as the concentration is increased. No evidence for a maximum in the degree of association, observed by Coughlan *et al.*, was found in the present study. Thus, the limiting molecular complexity of three observed here is in line with the accepted view that the n-alkyl titanates are trimeric in the pure state.

The existence of monomeric and trimeric entities in benzene solution is established by the present work and, since effective collisions between three monomer molecules are likely to be uncommon, the dissociation is here visualized as a two-step reaction:

$$M_3 \rightleftharpoons M_2 + M_1 \quad (1)$$

$$M_2 \rightleftharpoons 2M_1 \quad (2)$$

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where M_3, M_2, and M_1 represent trimer, dimer, and monomer, respectively. The equilibrium constants K_1 and K_2 for reactions (1) and (2) can be written:

$$K_1 = [M_2][M_1]/[M_3] \quad (3)$$

and

$$K_2 = [M_1]^2/[M_2] \quad (4)$$

If M_0 represents the mass of tetrabutoxytitanium added to the benzene solution, then

$$[M_0] = 3[M_3] + 2[M_2] + [M_1], \quad (5)$$

or from equations (3) and (4), we have

$$[M_0] = \frac{3[M_1]^3}{K_1K_2} + \frac{2[M_1]^2}{K_2} + [M_1], \quad (6)$$

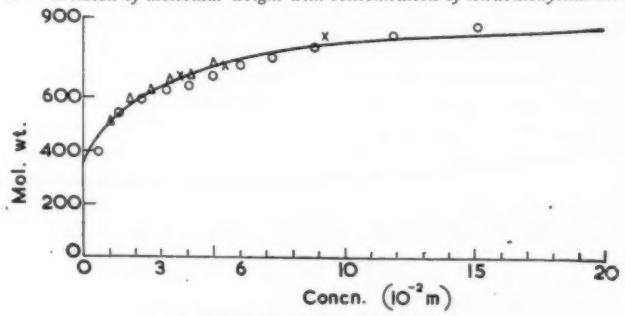
from which the relative concentrations of M_1, M_2, and M_3 can be calculated if K_1 and K_2 are known.

The experimental results can be fitted by trial-and-error selection of values for K_1 and K_2; it is found that there is a good fit only when K_2 is increased to such a value that the concentration of M_2 becomes negligible; equation (6) then reduces to

$$[M_0] = 3[M_1]^3/K + [M_1]. \quad (7)$$

Selecting $K = 1 \times 10^{-4}$ gives a calculated curve (see Fig. 1) which fits the experimental results closely, and confirms the view that the maxima observed by Coughlan *et al.* are

FIG. 1. *Variation of molecular weight with concentration of tetrabutoxytitanium*(IV).



Curve, calc. for $K = 1 \times 10^{-4}$.

incompatible with a reasonable model for the system. The dissociation of tetrameric methoxythallium(I) in benzene was found by Sidgwick and Sutton [7] to give a similar curve.

While equation (7) represents a reaction of the third order, it is extremely unlikely that the association of M_1 to M_3 involves an effective three-bodied collision, and it is more reasonable to assume that the reactions involving M_1 are really bimolecular. Since K_2 is very large, the dimer M_2 is unstable with respect to the monomer M_1.

Successive replacement of butoxy-groups by the more electronegative chlorine has a profound influence on the association equilibrium. Replacement of one group so stabilizes the trimer that no dissociation is observed at concentrations where tetrabutoxytitanium is nearly completely dissociated (cf. Fig. 2). This suggests that the positive charge, and hence acceptor properties, of the central titanium atom have been increased, with concomitant increase in the strength of the alkoxy-bridge. Dichlorodibutoxytitanium, $TiCl_2(OBu)_2$, is dimeric and also does not dissociate in the concentration range examined

(cf. Fig. 2). Butoxytrichlorotitanium, $TiCl_3$·OBu, like titanium tetrachloride, is monomeric and displays no tendency to associate. Coughlan *et al.* reported a limiting association number of three for chlorotriethoxytitanium, $TiCl(OEt)_3$, in benzene.

The Strength of the Intermolecular Butoxy-bridge.—Dissociation of tetrabutoxytitanium(IV) was also followed calorimetrically, by measuring the variation, with concentration, of its heat of solution in benzene at 30°. The reaction is endothermic since rupture of intermolecular butoxy-bridges is involved; the heat absorbed per mole of ester is plotted against concentration in Fig. 3.

FIG. 2. *Molecular weights of alkoxytitanium chlorides.*

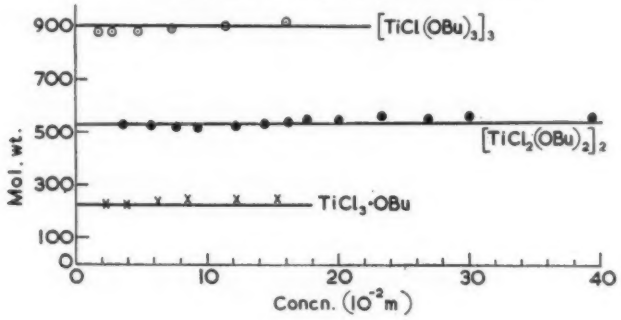
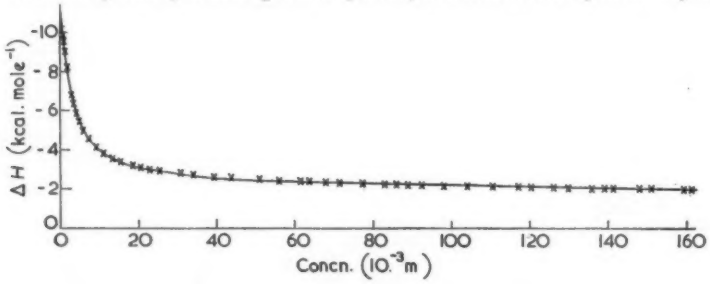


FIG. 3. *Variation of heats of solution (per mole of solute) with concentration of tetrabutoxytitanium*(IV).



The total energy change (ΔH), when the pure liquid trimer is completely dissociated and solvated in benzene solution, can be estimated by extrapolating the curve to zero concentration, giving a value *ca.* 11 kcal./mole. The major factors contributing to this are likely to be the heat of solution of the trimer in benzene, ΔH_S, M_3 (liquid) $\rightleftharpoons$ M_3 (solution), and the energy required to dissociate the trimer to the monomer, ΔH_B, M_3 (solution) $\rightleftharpoons$ $3M_1$ (solution), where ΔH_S and ΔH_B are expressed per titanium atom. For the present purpose, it is assumed that the interaction forces between titanium and benzene are small and independent of the state of aggregation. It follows that at a given concentration,

$$Q \approx [M_1]\Delta H_B + [M_0]\Delta H_S. \qquad (8)$$

The experimental results can again be closely fitted, by trial-and-error methods, by selecting $\Delta H_S = 1{\cdot}24$ kcal./mole and using 4×10^{-6} as the equilibrium constant defined by equation (7). The experimental result, Q, the values of $[M_1]\Delta H_B$ obtained from equation (8), and those calculated from equation (7) are compared in Fig. 4.

It is also possible to obtain an independent but approximate value for ΔH_B from the two equilibrium constants, $K_{5{\cdot}5°}$ (cryoscopic), and $K_{30°}$ (calorimetric), and to compare

this value with that obtained by extrapolation of the ΔH curve. Application of the integrated form the van't Hoff equation gives $-\Delta H_B \approx 8$ kcal./mole, which may be compared with the value 9·8 kcal./mole (*i.e.*, 11 — ΔH_S kcal./mole) obtained by extrapolation of the experimental heats of solution to zero concentration. The agreement is

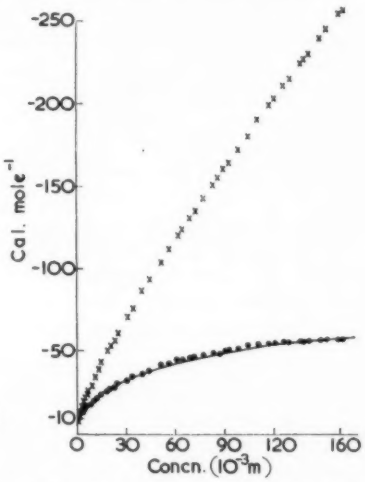


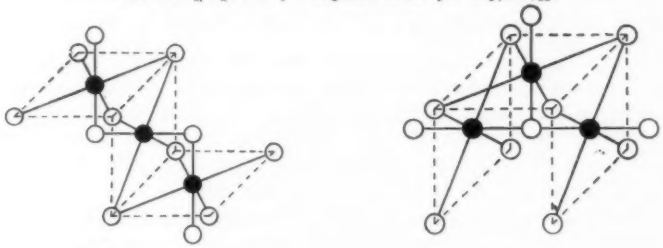
FIG. 4. *Q and* $[M_1]\Delta H_B$ *as a function of concentration of tetrabutoxytitanium*(IV).
× Exptl. *Q*. ● Exptl. $Q - 1{\cdot}24[M_0]$.
Curve: Calc. for $M_1 \times 9{\cdot}76$; $K = 4 \times 10^{-6}$.

satisfactory in view of the implicit assumptions, and in particular it is unlikely that solvent–solute interaction (ΔH_S) is the same for both the monomer and the trimer.

The present value for the intermolecular-bridge energy, 9·8 kcal./mole, resembles the *ca.* 10 kcal./mole estimated by Bradley *et al.*[1] for tetraethoxytitanium. If the structure of the trimer involves two alkoxy-bridges per titanium atom, each alkoxide bridge will contribute 4·9 kcal./mole. This value is similar in magnitude to the energy of a hydrogen bond [8] and suggests that the intermolecular bonding in n-alkyl titanates is predominantly electrostatic (cf. formula 1b).

Structures.—The present work has confirmed the view that tetrabutyl titanate associates by means of weak intermolecular titanium–oxygen bonds, and that polymerization

Structures proposed by Coughlan et al.[4] *for* $Ti_3(OR)_{12}$.



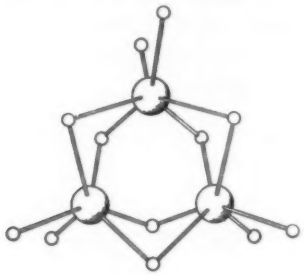
(II) (III)

● Ti. ○, O in OR.

ceases abruptly at the trimer. Coughlan *et al.* ascribed the association to the tendency of quadrivalent titanium to attain a six-covalent environment, as, for example, in rutile or anatase. They suggested that each pair of titanium atoms was supported by three-bridging alkoxy-groups, giving alternative structures (II) and (III), which are based on

[8] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, 1948, p. 284.

the stacking of three TiO_6 octahedra face to face. Structure (III) necessitates a four co-ordinated square-planar oxygen atom attached to three titanium atoms and one alkyl group, and for this reason is considered here to be untenable. Structure (II) has been widely accepted and in particular, the group working at Birkbeck College [3,9] have stressed this arrangement when discussing the hydrolysis of n-alkyl titanates. This model is



Proposed cyclic structure for $Ti_3(OR)_{12}$ *based on* TiO_6 *trigonal prisms.*

(IV)

attractive as it is consistent with a co-ordination number of six for all the titanium atoms and limits the maximum association to three monomer units. However, a disadvantage is an inherent asymmetry which necessitates the central titanium atom being surrounded by six butoxy-bridges with the remaining titanium atoms each carrying three terminal and three butoxy-bridges. The need for high symmetry becomes apparent in the interpretation of the structure of trimeric tributoxychlorotitanium, $Ti_3Cl_3(OBu)_9$, where a triangular, rather than a linear, arrangement of the metal atoms would provide a higher natural symmetry and enable one chlorine atom to be bound to each titanium atom.

Two stereochemical arrangements incorporating this concept have been proposed by the present authors.[10] One is based on a six-covalent oxygen environment for titanium, but a trigonal prismatic, rather than an octahedral, arrangement of the TiO_6 group is envisaged. This leads to structure (IV) in which two "bridge" and two "terminal" alkoxy-groups per titanium atom are present. A scale model reveals that twelve n-alkyl groups can be nicely accommodated about the three titanium atoms; it can accommodate either one or two terminal chlorine atoms per titanium atom and retain a high degree of symmetry.

The higher stability of $Ti_3Cl_3(OBu)_9$ than of $Ti_3(OBu)_{12}$ probably arises from the greater induced positive charge ($\delta+$) on the metal leading to stronger intermolecular bonding ($\overset{\delta+}{Ti}-\overset{\delta-}{O}\cdots\overset{\delta+}{Ti}$). From this point of view the stabilities of dibutoxydichlorotitanium and butoxytrichlorotitanium might be expected to increase with increasing chlorine content, if no steric interactions occur. In fact, neither ester is trimeric, but dibutoxydichlorotitanium is dimeric, $Ti_2Cl_4(OBu)_4$, and displays no tendency to dissociate (or associate), while the trichloro-compound $TiCl_3{\cdot}OBu$, like titanium tetrachloride, remains monomeric at all concentrations studied.

The monomeric nature of butoxytrichlorotitanium may well be evidence that a minimum number of two alkoxy-groups per titanium is a prerequisite for association, in harmony with both the structures (II) and (IV). If so, then titanium must exhibit six-covalency in its alkoxychloro-derivatives but their structure cannot be based on an octahedral stereochemistry for titanium. However, the above evidence is not unambiguous, for the inability of butoxytrichlorotitanium to associate may be a further manifestation of redistribution in electron density due to introduction of chlorine. Thus, the presence of three chlorine atoms may exert a cumulative inductive effect on titanium sufficiently large

[9] Bradley, Gaze, and Wardlaw, *J.*, 1955, 3977.
[10] Martin and Winter, *Nature*, 1960, **188**, 313.

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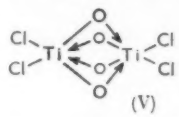
to induce appreciable p_π–d_π bonding between the oxygen and titanium atoms and under these conditions association would not be expected. It seems unlikely that the steric effect of three chlorine atoms would be sufficient to hinder association, for titanium tetrachloride is known to form adducts with a large number of donor molecules.

The structure of the dimeric species, $Ti_2Cl_4(OBu)_4$, is open to speculation, but the high stability is consistent with a structure such as (V) which is based on a minimum requirement of two alkoxy-bridges per titanium atom. This requires a two-bodied collision of tetrahedral monomers and only a small rearrangement of bond angles. Further association to a trimer (IV) by collision with a third monomer would necessitate rupture of two bridges already stabilized by the high positive charge on the titanium. In this structure each titanium atom is involved in a six-covalent environment based on $TiCl_2O_4$ trigonal prisms sharing a common face.

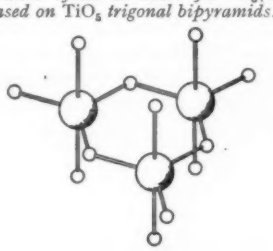


(V)

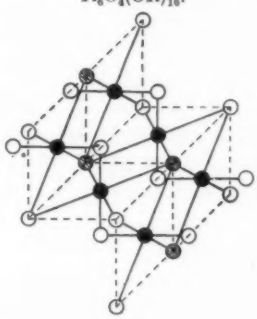
The cryoscopic and calorimetric results show that the dimer of tetrabutoxytitanium is relatively unstable; electronegative chlorine substituents are apparently necessary to stabilize structure (V). The positive charge induced on titanium by only one chlorine atom seems, however, insufficient to stabilize the dimer, and a further collision with monomer leads to the trimer in which the bond angles are somewhat more favourable for a strain-free structure.

This interpretation is based on the concept that titanium achieves covalent saturation with a co-ordination number of six. Andersson and Wadsley [11] recently established by *X*-ray methods that quadrivalent titanium is five-covalent in the mixed oxide $K_2Ti_2O_5$. The TiO_5 grouping is trigonal bipyramidal, and on this basis they have suggested to us that structure (VI) provides an alternative stereochemical arrangement for $Ti_3(OBu)_{12}$ and $Ti_3Cl_3(OBu)_9$. This differs from structure (IV), not only in the five-covalency of titanium, but also in that only one alkoxy-bridge per titanium is present.

Alternative cyclic structure for $Ti_3(OR)_{12}$ *based on* TiO_5 *trigonal bipyramids.*


(VI)

Structure proposed by Bradley et al.[9] *for* $Ti_6O_4(OR)_{16}$.


(VII)

● Ti. ○ O in OR. ◉ O in Ti–O–Ti.

Hydrolysis of Titanium Alkoxides.—Bradley and his co-workers[3,9] studied the hydrolysis of the alkoxides in boiling butanol, a strong donor solvent, and established that the titanium oxide alkoxides, $TiO_n(OR)_{4-2n}$, formed are low polymers such as $Ti_6O_4(OR)_{16}$ and $Ti_{12}O_{12}(OR)_{24}$. These products were explained in terms of interaction of water with structure (II) to give a structure such as (VII) for $Ti_6O_4(OR)_{16}$. A polymerization of this kind would require a statistically unfavourable mutual orientation of two partly hydrolysed $Ti_3(OH)_4(OR)_8$ units before effective collision and expulsion of four water molecules could occur, and would require also the preferential hydrolysis of two terminal and two bridging

[11] Andersson and Wadsley, *Nature*, 1960, **187**, 499.

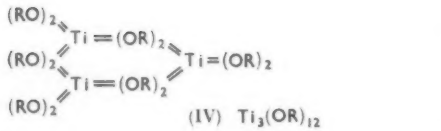
alkoxide groups from only one edge of the parent trimer. Further, it involves an unknown four-covalent bonding arrangement between oxygen and its nearest four titanium neighbours.

A hydrolysis mechanism based on the cyclic model (IV) can still logically lead to titanium oxide alkoxide polymers $TiO_n(OR)_{4-2n}$, yet is more amenable to kinetic interpretation. Hydrolysis of terminal alkoxy-groups, intermolecular elimination of alcohol, and intramolecular elimination of water are suggested as likely successive stages. Such a mechanism involves a kinetically simple two-point collision, and a possible scheme would be as follows (b = bridge; t = terminal group):

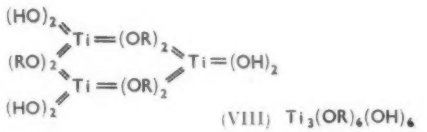
(i) $Ti_3(OR)_6{}^b(OR)_6{}^t + 6H_2O \longrightarrow Ti_3(OR)_6{}^b(OH)_6{}^t + 6ROH$ (see structure VIII)

(ii) $Ti_3(OR)_6{}^b(OH)_6{}^t + Ti_3(OR)_6{}^b(OR)_6{}^t \longrightarrow (RO)_4{}^t(RO)_6{}^bTi_3(O)_2{}^bTi_3(OR)_6{}^b(OH)_4{}^t + 2ROH$ (see structure IX)

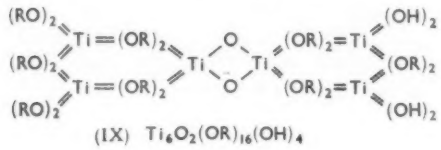
(iii) $(RO)_4{}^t(RO)_6{}^bTi_3(O)_2{}^bTi_3(OR)_6{}^b(OH)_4{}^t \longrightarrow (RO)_4{}^t(RO)_6{}^bTi_3(O)_2{}^bTi_3(OR)_6{}^b(O)_3{}^t + 2H_2O$ (see structure X)



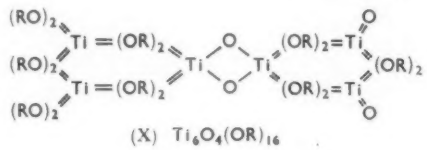
(IV) $Ti_3(OR)_{12}$



(VIII) $Ti_3(OR)_6(OH)_6$



(IX) $Ti_6O_2(OR)_{16}(OH)_4$



(X) $Ti_6O_4(OR)_{16}$

The structures of the participating entities are represented diagrammatically by (IV), (VIII), (IX), and (X). Further hydrolysis of $Ti_6O_4(OR)_{16}$ by this mechanism could lead to polymers such as $Ti_9O_8(OR)_{20}$ and $Ti_{12}O_{12}(OR)_{24}$ as observed by Bradley and his colleagues.*

Whether the titanium is five- or six-covalent, octahedral or trigonal prismatic, must rest on a complete structure analysis. However, it is suggested that a structure based on a triangular rather than a linear arrangement of the titanium atoms is more consistent with the known chemistry of n-alkyl titanates.

Experimental

Tetrabutoxytitanium(IV).—This compound was prepared as described by Kraitzer, McTaggart, and Winter.[12] It was always freshly distilled before use (Found: TiO_2, 23·5. Calc. for $C_{16}H_{36}O_4Ti$: TiO_2, 23·5%).

Chlorotributoxytitanium(IV).—This was prepared by treatment of 1·0 equiv. of tetrabutoxytitanium with 0·9 equiv. of acetyl chloride, followed by distillation and fractionation of the crude ester at 1 mm. (Found: TiO_2, 26·9; Cl, 11·7. Calc. for $C_{12}H_{27}ClO_3Ti$: TiO_2, 26·4; Cl, 11·7%).

Dichlorodibutoxytitanium(IV).—Titanium tetrachloride (1·0 equiv.) was added slowly to butan-1-ol (2·0 equiv.) with cooling. Hydrogen chloride formed was removed under reduced pressure, and the crude ester distilled and fractionated at 1 mm. (Found: TiO_2, 29·9; Cl, 26·8. Calc. for $C_8H_{18}Cl_2O_2Ti$: TiO_2, 30·2; Cl, 26·8%).

Trichlorobutoxytitanium(IV).—The ester, prepared from titanium tetrachloride (1·0

* For a further discussion concerning the structures of tetra-alkyl titanates and their hydrolysis products, see Bradley and Westlake, and Martin and Winter (*Nature*, 1961, in the press).

[12] Kraitzer, McTaggart, and Winter, *J. Council Sci. Ind. Res. Australia*, 1948, **21**, 328.

equiv.) in hexane with butan-1-ol (1·0 equiv.), was twice washed with hexane and twice crystallized from benzene (Found: TiO_2, 35·6; Cl, 46·3. Calc. for $C_4H_9Cl_3OTi$: TiO_2, 35·6; Cl, 46·8%).

Benzene.—Benzene used for the cryoscopic and calorimetric work was purified by treating it five times with concentrated sulphuric acid, washing it until neutral, and drying it (Na_2SO_4, then CaH_2). It was distilled through a column (*ca.* 80 theor. plates), and the fractions freezing at 5·48° (or better) were combined and fractionally crystallized.

Cryoscopy.—The classical Beckmann procedure was found to be too insensitive for the present measurements, since dissociation of alkyl titanates in benzene commences at very low

FIG. 5a. *Cryoscope.*

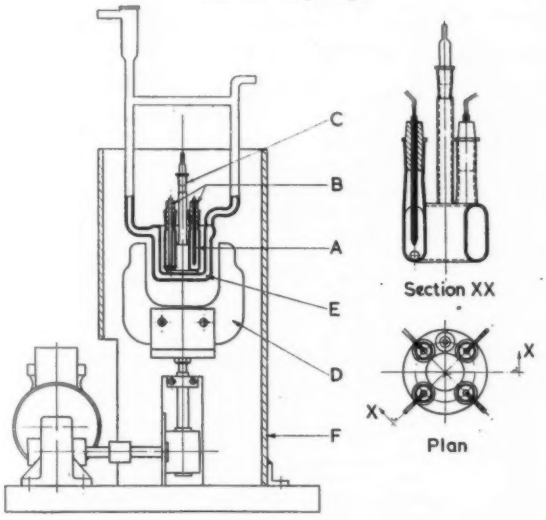
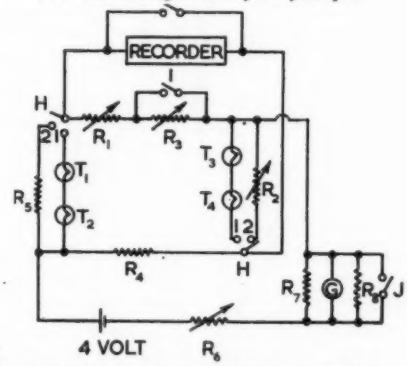


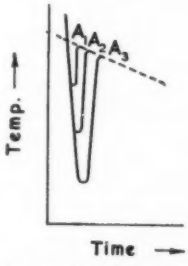
FIG. 5b. *Bridge circuit for cryoscope.*



T_1, T_2, T_3, T_4, Thermistors type F2311. R_1, R_2, 0—10^4 Ω Decade box. R_3, 0—10^3 Ω Decade box. R_4, R_5, $7·5 \times 10^3$ Ω Wire wound resistance. R_6, 2×10^3 Ω Potentiometer. R_7, 20·8 Ω Wire wound resistance. R_8, 1×10^3 Ω Resistance. G, Spot galvanometer. H, Double pole, double-throw switch. I, J, Single pole switch.

concentrations. A more sensitive apparatus was developed which permitted exclusion of moisture and minimized errors due to irregular supercooling. The apparatus (Fig. 5) consisted of a ring shaped cell (A) to which were attached four B/10 sockets (B) and one B/7 socket (C). Accurately shaped and drilled Teflon cones, each holding one thermistor (Stantel F2311), were inserted at B in such a way that the tips of the thermistors were approximately 5 mm. below the liquid level. The opening (C) which served for filling and for the addition of the samples was stoppered with a sealed B/7 male cone. To avoid ingress of moisture the joints were protected with serum caps. Mixing was by a glass-covered steel ball moved by a magnet (D) (100 r.p.m.). Supercooling was minimized by provision of finely powdered glass sintered along the path of the ball. Cooling was by water at 1·5° ± 0·05° passed through the jacket (E). Rubber spacer-rings prevented direct contact of the cell with the jacket. During operation the top of the cell and jacket was covered with cotton wool. The whole assembly was surrounded by a shield (F) made from 1/8 in. steel plate, to eliminate magnetic interference with the electrical circuit.

FIG. 6.



The variation in resistance of the thermistors with change in temperature was measured by means of a Wheatstone bridge and recorded automatically on a Varian recorder. The applied current (0·5 milliamp.) was measured by a damped galvanometer (G). Adjustments could be made with the potentiometer (R_6). Drifts in the circuit could be observed and allowed for by disconnecting the thermistors through switch (H) and replacing them by the two resistances R_2 and R_5. The degree of supercooling was measured by operating the decade box (R_3)

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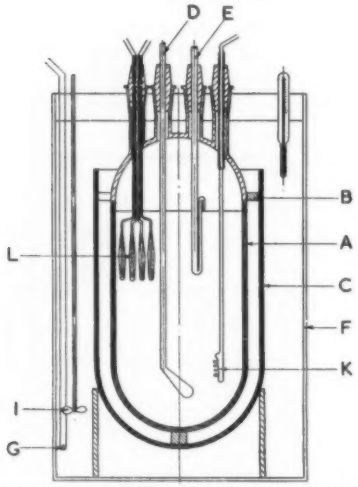
which could be short-circuited by means of switch (I) immediately after crystallization had commenced.

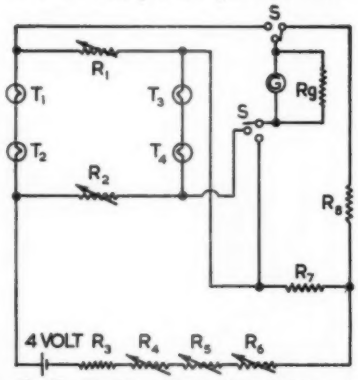
In the classical cooling-curve method, the true freezing point is determined by extrapolating the freezing-point curve to zero supercooling. Provided the concentration of the solute is not very large and the freezing is not allowed to proceed for too long, very little difficulty is met owing to the non-linearity of this curve. If, however, the sensitivity of the temperature-measuring device is increased, as with the present instrument, the non-linearity is accentuated

FIG. 7a. *Calorimeter.*



A, 1-l. vacuum-jacketted vessel. B, Cork ring. C, 3-l. open-mouthed Dewar flask. D, Stirrer (*ca.* 100 r.p.m.). E, Pipette for addition of sample. F, Oil-bath. G, Heater. I, Stirrer. K, Calibration coil (*ca.* 50 ohms). L, Thermistors (Stantel F2311).

FIG. 7b. *Bridge circuit for calorimeter.*



T_1, T_2, T_3, T_4, Thermistors type F2311. R_3, R_9, 10,000 Ω Resistance. R_1, R_2, 10,000 Ω Decade box. R_4, 10,000 Ω Potentiometer. R_5, 1000 Ω Potentiometer. R_6, 100 Ω Potentiometer. R_7, 2·4 Ω Resistance. R_8, 4000 Ω Resistance. S, Double pole, double-throw switch. G, Cambridge galvanometer; 450 Ω resistance.

to such a degree that extrapolation becomes impossible. To overcome this a different approach was chosen to determine the true freezing point at zero supercooling. The maximum temperature reached by the system (A_1, A_2, A_3 in Fig. 6) was found to be a linear function of the degree of supercooling. When this relationship had been established for each solute concentration, no difficulty in extrapolation was encountered provided the degree of supercooling was not too great.

The method was evaluated by molecular-weight determinations on a number of pure organic compounds, with azobenzene as a calibrant. The results are shown in Table 2.

TABLE 2. *Accuracy of cryoscopic technique*

Compound	Concn. range (10^{-2} m)	Mol. wt. found	Mol. wt. calc.	No. of detns.
Biphenyl	1·03—11·69	158·5	154·2	8
Me stearate	1·08—8·09	296·2	298·5	5
1-Chloro-2,4-dinitrobenzene	3·50—8·84	209·4	202·5	3
Ph benzoate	1·31—12·98	200·0	198·5	7
Naphthalene	1·35—15·92	131·9	128·2	10

Heats of Solutions.—The heats of solution were measured in a calorimeter of 1-l. capacity as shown in Fig. 7. Variations in the resistance of the thermistors were measured with a Wheatstone bridge which incorporated a circuit for checking accurately the stability of the current applied. The optical arm of the galvanometer was 3·6 m. A galvanometer deflection

of 1 mm. corresponded to approximately 1×10^{-4} °. Calibration was effected by applying an accurately measured current to the heating coil.

The authors are grateful to Dr. H. W. W. Brett for frequent and helpful discussions.

CENTRAL RESEARCH LABORATORIES,
IMPERIAL CHEMICAL INDUSTRIES OF AUSTRALIA AND NEW ZEALAND LIMITED,
MELBOURNE, AUSTRALIA. [*Received, December 29th*, 1960.]

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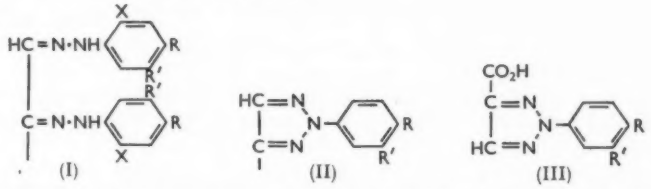
567. *The Scope and Mechanism of Carbohydrate Osotriazole Formation. Part V.*[1] *Chloro- and Iodo-phenylosotriazoles.*

By H. EL KHADEM, ZAKI M. EL-SHAFEI, and M. H. MESHREKI.

o-Chloro- and *o*-iodo-phenylosazones are dehalogenated when converted into osotriazoles by copper sulphate. Chlorine-water converts osazones into osotriazoles and chlorinates them in the 4-position (if free). Iodine converts osazones into osotriazoles but does not halogenate them. Halogen exchange occurs when iodophenylosazones are converted into triazoles with bromine but not with chlorine or iodine.

IT has been shown [1] that copper precipitated during the conversion of osazones into osotriazoles, by means of copper sulphate, removed *o*-bromo-substituents. For a similar reaction with chloro- and iodo-derivatives, glucose *o*-chloro- (I; R = R′ = H, X = Cl) and *o*-iodo-phenylosazone (I; R = R′ = H, X = I) were prepared and refluxed with aqueous copper sulphate. Here, too, *ortho*-dehalogenation took place and glucose phenylosotriazole (II; R = R′ = H) was produced.



o-Halogenobenzoic acids were likewise dehalogenated by a refluxing aqueous suspension of copper powder. Apart from *o*-bromobenzoic acid investigated by Hurtley,[2] we found that *o*-chlorobenzoic acid yielded benzoic acid. The *o*-iodo-acid, on the other hand, lost its iodine rapidly, yielding biphenic acid by the Ullmann reaction. Dehalogenation of *o*-halogeno-phenylosotriazoles and -benzoic acids is probably due to location of the halogen atom *ortho* to an electron-attracting group which would facilitate the removal of the halogen cation, leaving a negative centre to be occupied by a hydrogen ion from the aqueous medium.

Chlorine water, like bromine water, converted osazones into osotriazoles and halogenated them in the 4-position. If this position was occupied, the osazones were merely converted into the osotriazoles. Thus, chlorine water converted glucose phenyl- (I; R = R′ = X = H) and *p*-chloro-phenylosazone (I; R = Cl, R′ = X = H) into the *p*-chlorophenylosotriazole (II; R = Cl, R′ = H) which was also obtained by the action of copper sulphate on glucose *p*-chlorophenylosazone. Glucose 3,4-dichloro- (II; R = R′ = Cl), 4-chloro-3-methyl- (II; R = Cl, R′ = Me), and 3-bromo-4-chloro-phenylosotriazole (II; R = Cl, R′ = Br) were also prepared by the action of chlorine-water on the *meta*-substituted osazones or by the action of copper sulphate on the disubstituted ones.

[1] Part IV, *J.*, 1960, 3993.
[2] Hurtley, *J.*, 1929, 1870.

Halogenation of triazoles in the 4-position is attributed to the electromeric effect of the approaching halogen cation which would cause a temporary shift of electrons from the triazole ring towards the *ortho*- and *para*-positions; owing to the steric effect of the triazole ring, substitution takes place in the *para*- and not in the *ortho*-position.

No halogen exchange took place when chloro- or bromo-phenylosazones were treated with bromine or chlorine respectively: glucose *p*-chlorophenylosazone yielded the *p*-chlorophenylosotriazole and the *meta*-isomer yielded the 4-bromo-3-chloro-phenylosotriazole (II; R = Br, R′ = Cl); glucose *p*-bromophenylosazone with chlorine yielded the *p*-bromophenylosotriazole, and the *meta*-isomer yielded the 3-bromo-4-chloro-phenylosotriazole (II; R = Cl, R′ = Br). In the case of iodophenylosazones, chlorine-water caused no exchange and glucose *p*-iodophenylosazone (I; R = I, R′ = X = H) yielded the corresponding *p*-iodophenylosotriazole (II; R = I, R′ = H); but when this osazone was treated with bromine water, an osotriazole was obtained which contained both iodine and bromine—it is probably a molecular compound. The *meta*-isomer also gave a product in which iodine was partially replaced by bromine.

Unlike chlorine and bromine, iodine in aqueous potassium iodide merely converted the osazones into osotriazoles without halogenating them. The reaction is also much slower, equiring 3 days for glucose *p*-methoxyphenylosazone, one week for glucose phenylosazone, and 2 and 3 weeks respectively for the *p*-iodo- and the *p*-bromo-phenyl derivative. Osazones having strong electron-attracting substituents such as nitro and carboxyl were unaffected by iodine. Also unaffected was glucose *p*-chlorophenylosazone, while the *meta*-isomer was only partially converted into the osotriazole after 3 weeks. This is in harmony with the view that triazole formation is inhibited by electron-attracting groups and facilitated by electron-donating ones.

Potassium permanganate readily converted glucose chloro- and iodo-phenylosotriazoles into chloro- and iodo-phenyl-1,2,3-triazole-4-carboxylic acid. As with bromine, 2-*m*-carboxyphenyl-1,2,3-triazole-4-carboxylic acid (III; R = H, R′ = CO_2H) resisted chlorination, probably because of $-I$ and $-T$ effects of the carboxyl group which render the 4-position deficient in electrons.

Treatment of 2-*m*-tolyl-1,2,3-triazole with potassium permanganate afforded 2-*m*-carboxyphenyl-1,2,3-triazole. The former was obtained by the action of copper sulphate on glyoxal bis-*m*-tolylhydrazone.

The ultraviolet absorption spectra of glucose *m*- and *p*-chloro- and *p*-iodo-phenylosotriazoles (II) and triazole-4-carboxylic acids (III) are characterised by a single peak between 272 and 278 mμ. On the other hand, osotriazoles and triazole-4-carboxylic acids having a 3-iodine substituent possess 2 peaks at 234—240 and 272—282 mμ. As with the osotriazoles and triazole-4-carboxylic acids studied earlier,[1] the peaks of the *para*-isomers are higher and shifted towards longer wavelengths. Similarly, the peaks for triazole-4-carboxylic acids are shifted more than for the corresponding osotriazoles. There is also a gradual shift towards longer wavelength for both the *meta*- and *para*-monosubstituted derivatives as we go from the chloro- through the bromo- to the iodo-substituents.

Experimental

Absorption spectra were determined for ethanolic solutions with a Unicam S.P. 500 spectrophotometer.

Glucose Osazones.—The osazones were prepared by adding an aqueous solution of glucose (10 g. in 100 ml.) to the calculated amount of the desired hydrazine hydrochloride and sodium acetate in water (300 ml.), followed by a few drops of acetic acid. The mixture was heated on the water-bath for the period shown and the *osazone* was filtered off (see Table 1). Unless otherwise stated, they were crystallised from dilute ethanol and were soluble in boiling ethanol or methanol and insoluble in water and ether.

Glucose Phenylosotriazole.—A solution of glucose *o*-chlorophenylosazone (5 g.) in dioxan (100 ml.) was refluxed with copper sulphate (5 g.) in water (100 ml.) for 4 hr., then filtered. To remove dioxan, the filtrate was distilled off until 100 ml. were collected. The residue was

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TABLE 1. *Substituted glucose phenylosazones.*

Subst. in Ph	Time (hr.)	M. p. (decomp.)	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N
o-Cl	2	230—232°	50	51·0	4·8	13·2	$C_{18}H_{20}Cl_2N_4O_4$	50·6	4·7	13·1
m-Cl	2	208	62	50·7	4·8	12·9	$C_{18}H_{20}Cl_2N_4O_4$	50·6	4·7	13·1
p-Cl	3	211	75	50·3	4·6	13·1	$C_{18}H_{20}Cl_2N_4O_4$	50·6	4·7	13·1
4-Br-3-Cl ...	2	206—207	35	36·9	3·2	9·5	$C_{18}H_{18}Br_2Cl_2N_4O_4$	36·9	3·1	9·6
4-Cl-3-Me...	2	184	52	—	—	12·2	$C_{20}H_{24}Cl_2N_4O_4$	—	—	12·3
3,4-Cl_2	4	192	73	43·0	4·0	11·4	$C_{18}H_{18}Cl_4N_4O_4$	43·5	3·6	11·3
o-I	2	176	56	35·3	3·3	8·6	$C_{18}H_{20}I_2N_4O_4$	35·4	3·3	9·2
m-I	3	198	24	36·0	3·5	8·9	$C_{18}H_{20}I_2N_4O_4$	35·4	3·3	9·2
p-I	2	Amorphous	—	—	—	—	—	—	—	—

concentrated on the water-bath; the crystals that separated (2 g.) recrystallised from water in needles, m. p. 195—196° alone or mixed with glucose phenylosotriazole [3] (Found: C, 54·9; H, 5·5; N, 16·0. Calc. for $C_{12}H_{15}N_3O_4$: C, 54·3; H, 5·7; N, 15·8%).

Glucose *o*-iodophenylosazone (5 g.), similarly treated, gave the same product (1·2 g.), m. p. and mixed m. p. 195° (Found: C, 54·0; H, 5·6; N, 15·7%).

Action of Copper Powder on o-*Halogenobenzoic Acids.*—A suspension of *o*-chlorobenzoic acid (5 g.) in water (200 ml.) was refluxed with freshly prepared copper powder (15 g.) for 3—4 hr., filtered, and acidified. Benzoic acid separated (2·4 g.); recrystallised from water, it had m. p. and mixed m. p. 121°.

A suspension of *o*-bromobenzoic acid, similarly treated, afforded the same acid.

A suspension of *o*-iodobenzoic acid (6 g.) in water (300 ml.) was refluxed with copper powder (20 g.) for 15 min. and treated as above. Biphenic acid separated (2·5 g.) having m. p. and mixed m. p. 227° (from water).

Glucose m-*Chlorophenylosotriazole.*—Glucose *m*-chlorophenylosazone (10 g.) was treated with copper sulphate (10 g.) for 4 hr. The crystals (4 g.) that separated recrystallised from water–ethanol in needles, m. p. 206—208°, soluble in ethanol and methanol and insoluble in ether and water (Found: C, 47·9; H, 4·6; N, 14·2; Cl, 11·7. $C_{12}H_{14}ClN_3O_4$ requires C, 48·1; H, 4·7; N, 14·0; Cl, 11·9%).

Glucose 4-*Bromo*-3-*chlorophenylosotriazole.*—Glucose *m*-chlorophenylosazone (5 g.) in water (150 ml.) was treated in the cold with bromine (6 ml.), and the mixture kept overnight. The reddish-brown mass obtained was filtered off and washed with water and ethanol (2·5 g.). *Glucose* 4-*bromo*-3-*chlorophenylosotriazole* recrystallised from ethanol in needles, m. p. 223° (solubility as above) (Found: C, 38·6; H, 3·5; N, 11·3. $C_{12}H_{13}BrClN_3O_4$ requires C, 38·1; H, 3·4; N, 11·1%).

Glucose 4-bromo-3-chlorophenylosazone (5 g.) was treated with copper sulphate (5 g.) as before. The osotriazole that separated was filtered off (2·2 g.) and recrystallised from ethanol in needles, m. p. and mixed m. p. 223° (Found: C, 38·3; H, 3·4; N, 11·0%).

Glucose 4-*Chloro*-3-*methylphenylosotriazole.*—Chlorine was bubbled into a suspension of glucose *m*-tolylosazone (10 g.) in water (250 ml.) for 1·5 hr. and the mixture kept overnight. The mass obtained was filtered off and washed with water and ethanol (4·5 g.). *Glucose* 4-*chloro*-3-*methylphenylosotriazole* recrystallised from water–ethanol in needles, m. p. 218° (solubility as above) (Found: C, 49·5; H, 4·9; N, 13·1; Cl, 11·7. $C_{13}H_{16}ClN_3O_4$ requires C, 49·8; H, 5·1; N, 13·4; Cl, 11·3%).

A suspension of glucose 4-chloro-3-methylphenylosazone (7 g.), in dioxan (150 ml.) and 3·5% aqueous copper sulphate (200 ml.), was refluxed for 1·5 hr. and filtered hot. Dioxan was removed as before and the osotriazole separated (2 g.); it recrystallised from water–ethanol in needles, m. p. and mixed m. p. 218° (Found: C, 49·6; H, 5·5; N, 13·1; Cl, 10·8%).

Glucose 3,4-*Dichlorophenylosotriazole.*—Chlorine was bubled into a suspension of glucose *m*-chlorophenylosazone (7 g.) in water (250 ml.) for 2·5 hr. and the mixture treated as above. The osotriazole (2·5 g.) recrystallised from ethanol in needles, m. p. 216° (solubility as above) (Found: C, 43·3; H, 3·8; N, 12·3; Cl, 20·9. $C_{12}H_{13}Cl_2N_3O_4$ requires C, 43·1; H, 3·9; N, 12·6; Cl, 21·3%).

Glucose 3,4-dichlorophenylosazone (10 g.) was treated with copper sulphate (10 g.) as before. The product (3 g.) recrystallised from ethanol in needles, m. p. and mixed m. p. 216° (Found: C, 43·2; H, 4·1; N, 12·3; Cl, 21·0%).

Glucose p-*Chlorophenylosotriazole.*—(*a*) A hot solution of glucose *p*-chlorophenylosazone

(5 g.) in dioxan (150 ml.) was refluxed with copper sulphate (5 g.) in water (100 ml.) for 4 hr., then filtered. Dioxan was removed as before. The *osotriazole* that separated (2·5 g.) recrystallised from ethanol in needles, m. p. 220° (solubility as for other osotriazoles) (Found: C, 48·3; H, 4·6; N, 13·9. $C_{12}H_{14}ClN_3O_4$ requires C, 48·1; H, 4·7; N, 14·0; Cl, 11·9%).

(*b*) Glucose *p*-chlorophenylosazone (2 g.) in water (100 ml.) was treated in the cold with bromine (4 ml.) as before. The mass obtained was filtered off, washed (1 g.), and recrystallised from ethanol, forming needles, m. p. and mixed m. p. 220° (Found: C, 48·4; H, 4·8; N, 14·4; Cl, 11·4%).

(*c*) Chlorine was bubbled into a suspension of glucose phenylosazone (2 g.) in water (100 ml.) for 2 hr. The mass formed was filtered off (1·2 g.) and recrystallised from ethanol (m. p. and mixed m. p. 220°) (Found: C, 47·7; H, 4·7; N, 14·3; Cl, 11·7%).

(*d*) A suspension of glucose *p*-chlorophenylosazone (2 g.) was treated with chlorine. The osotriazole (1 g.), recrystallised from ethanol, had m. p. and mixed m. p. 220° (Found: C, 48·1; H, 5·1; N, 14·2; Cl, 11·7%).

Glucose p-*Chlorophenylosotriazole Tetra-acetate*.—A solution of the osotriazole in dry pyridine was treated with acetic anhydride; the *tetra-acetate* crystallised from methanol in needles, m. p. 108° (Found: C, 51·8 H, 4·9; N, 9·3. $C_{20}H_{22}ClN_3O_8$ requires C, 51·4; H, 4·7; N, 9·0%).

Glucose m-*Iodophenylosotriazole*.—A suspension of glucose *m*-iodophenylosazone (10 g.) in dioxan (200 ml.) was treated with 5% aqueous copper sulphate (200 ml.) as before. The *osotriazole* (1·5 g.) recrystallised from water–ethanol in needles, m. p. 223° (solubility as above) (Found: C, 36·9; H, 3·6; N, 10·8. $C_{12}H_{14}IN_3O_4$ requires C, 36·8; H, 3·6; N, 10·7%).

Glucose p-*Iodophenylosotriazole*.—Glucose *p*-iodophenylosazone (10 g.) was treated with copper sulphate (10 g.) as for the *meta*-isomer. On concentration, the *osotriazole* separated (2·5 g.); it recrystallised from dilute ethanol in needles, m. p. 240—242° (solubility as above) (Found: C, 37·0; H, 3·6; N, 10·4%).

A cold suspension of glucose *p*-iodophenylosazone (10 g.) was treated with chlorine as above. The osotriazole (4 g.) recrystallised from dilute ethanol in needles, m. p. and mixed m. p. 240—242° (Found: C, 37·2; H, 3·7; N, 10·2%).

Action of Bromine on Glucose p-*Iodophenylosazone*.—A cold suspension of glucose *p*-iodophenylosazone (10 g.) in water (150 ml.) was treated with bromine (5 ml.) as above. The mass formed was filtered off and washed with water and ethanol (6 g.). On crystallisation from ethanol, a mixed triazole was obtained (Found: C, 39·2; H, 3·6; N, 11·7; Br, 10·7; I, 17·7. Calc. for $C_{12}H_{14}BrN_3O_4$,$C_{12}H_{14}IN_3O_4$: C, 39·2; H, 3·8; N, 11·5; Br, 10·9; I, 17·3%).

Glucose 3-*Bromo*-4-*chlorophenylosotriazole*.—Glucose *m*-bromophenylosazone (4 g.), treated with chlorine as before, gave this *osotriazole* (1 g.), needles (from ethanol), m. p. 212° (Found: N, 11·2; Cl, 9·6; Br, 20·6. $C_{12}H_{13}BrClN_3O_4$ requires N, 11·1; Cl, 9·4; Br, 21·1%).

TABLE 2. *Formation of osotriazoles by iodine.*

Subst. in Ph of glucose phenyl-osotriazole	Time (days)	M. p. and mixed m. p.	Yield (%)	Found (%)				Calculated (%)		
				C	H	N	Formula	C	H	N
Unsubst.	7	195° [3]	67	54·6	5·7	15·9	$C_{12}H_{15}N_3O_4$	54·3	5·7	15·8
m-I	14	223	65	36·6	3·5	10·5	$C_{12}H_{14}IN_3O_4$	36·8	3·6	10·7
p-I	14	240—242	78	36·9	3·7	10·6	$C_{12}H_{14}IN_3O_4$	36·8	3·6	10·7
m-Me	10	195 [5]	70	55·6	6·1	15·5	$C_{13}H_{17}N_3O_4$	55·9	6·1	15·1
p-Me	7	207 [6]	64	55·7	6·0	15·0	$C_{13}H_{17}N_3O_4$	55·9	6·1	15·1
p-MeO	3	200 [1]	85	52·9	6·0	14·1	$C_{13}H_{17}N_3O_5$	52·9	5·7	14·2
m-Br	11	209—210 [5]	68	42·0	4·4	11·8	$C_{12}H_{14}BrN_3O_4$	41·9	4·1	12·2
p-Br	21	225—227 [4]	60	42·1	4·3	11·9	$C_{12}H_{14}BrN_3O_4$	41·9	4·1	12·2

Glucose p-*Bromophenylosotriazole*.—Glucose *p*-bromophenylosazone (3 g.) was treated with chlorine as before. The *p*-bromo-osotriazole was filtered off (1 g.) and recrystallised from ethanol in needles, m. p. and mixed m. p. 225—227° [4] (Found: C, 42·0; H, 4·2; N, 12·0; Br, 23·6. Calc. for $C_{12}H_{14}BrN_3O_4$: C, 41·9; H, 4·1; N, 12·2; Br, 23·3%).

Glucose p-*Carboxyphenylosotriazole*.—Glucose *p*-carboxyphenylosazone, similarly treated with chlorine, yielded glucose *p*-carboxyphenylosotriazole, m. p. and mixed m. p. 268° [1] (Found: C, 50·3; H, 4·9; N, 13·4. Calc. for $C_{13}H_{15}N_3O_6$: C, 50·5; H, 4·9; N, 13·6%).

[3] Hann and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 735.
[4] Hardegger, El Khadem, and Schreier, *Helv. Chim. Acta*, 1951, **34**, 253.
[5] El Khadem and El-Shafei, *J.*, 1959, 1655.
[6] Hardegger and El Khadem, *Helv. Chim. Acta*, 1947, **30**, 1478.

Formation of Osotriazoles by the action of Iodine.—The osazone (1 g.) was suspended in a solution of iodine (10 g.) in 10% aqueous potassium iodide (100 ml.) and left at room temperature for the period shown with occasional shaking. The osotriazole was filtered off and recrystallised from water–ethanol.

2-*Aryl*-1,2,3-*triazole*-4-*carboxylic Acids.*—A boiling suspension of the osotriazole (1—2 g.) in water (100—200 ml.) was treated with potassium permanganate (3—6 g.) until the pink colour persisted. The hot mixture was filtered, treated with sodium hydrogen sulphite, and acidified. The *acid* which separated recrystallised from water–ethanol; it was soluble in ethanol or methanol and insoluble in water (see Table 3).

Glyoxal Bis-m-*tolylhydrazone.*—Polymerised glyoxal [7] (25 g.) was thoroughly mixed with phosphorus pentoxide (15 g.) and heated with a flame. Monomeric glyoxal distilled and was collected in a trap cooled with solid carbon dioxide and acetone.[8] It was treated with a solution of *m*-tolylhydrazine (15 g.) in water (200 ml.) and acetic acid (10 ml.) and then heated at 40° for 10 min. The *bishydrazone* that separated (3 g.) recrystallised from dilute ethanol in yellow

TABLE 3. *Aryl*-1,2,3-*triazole*-4-*carboxylic acids.*

		Yield	Found (%)				Required (%)		
Subst. in Ph	M. p.	(%)	C	H	N	Formula	C	H	N
m-Cl	202—204°	54	48·6	2·6	19·2	$C_9H_6ClN_3O_2$	48·3	2·7	18·8
p-Cl	232	30	48·3	2·6	18·8	$C_9H_6ClN_3O_2$	48·3	2·7	18·8
3-Br-4-Cl	215	43	—	—	14·1	$C_9H_5BrClN_3O_2$ *	—	—	13·9
4-Br-3-Cl	222	62	36·0	1·7	13·8	$C_9H_5BrClN_3O_2$	35·7	1·7	13·9
3,4-Cl_2	216—217	54	42·2	2·0	15·7	$C_9H_5Cl_2N_3O_2$	41·9	1·9	16·3
m-I	201	50	34·2	2·0	13·6	$C_9H_6IN_3O_2$	34·3	1·9	13·3
p-I	265	55	34·4	2·0	13·0	$C_9H_6IN_3O_2$	34·3	1·9	13·3
4-Cl-3-CO_2H	273—274	58	45·1	2·3	15·6	$C_{10}H_6ClN_3O_4$	44·9	2·2	15·7

* Found: Cl, 12·0; Br, 23·6. Reqd.: Cl, 11·7; Br, 26·4%.

plates, m. p. 136° (decomp.), soluble in ethanol, methanol, and ether and insoluble in water (Found: C, 72·0; H, 6·7; N, 21·0. $C_{16}H_{18}N_4$ requires C, 72·2; H, 6·8; N, 21·0%).

2-m-*Tolyl*-1,2,3-*triazole.*—Glyoxal bis-*m*-tolylhydrazone (3 g.) was refluxed in a solution of copper sulphate (4 g.) in 20% aqueous dioxan (200 ml.) for 1·5 hr. The solution was then steam-distilled and the distillate (200 ml.) extracted with ether. The ethereal layer was washed with dilute hydrochloric acid and dried (Na_2SO_4). The triazole (1 g.) remaining after removal of the ether was used for the preparation of the corresponding acid without purification.

2-m-*Carboxyphenyl*-1,2,3-*triazole.*—To a boiling suspension of 2-*m*-tolyl-1,2,3-triazole (1 g.) in water (250 ml.), potassium permanganate (4·0 g.) was added and the mixture treated as before. The *acid* which separated (0·6 g.) recrystallised from water–ethanol in needles, m. p. 205—207° (Found: C, 57·2; H, 4·1; N, 22·0. $C_9H_7N_3O_2$ requires C, 57·1; H, 3·7; N, 22·2%).

Spectra.—These are recorded in Table 4.

TABLE 4. *Ultraviolet spectra.*

Osotriazole (II)						Triazole (III)					
R	R′	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{min.}$ (mμ)	log ε	R	R′	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{min.}$ (mμ)	log ε
Cl	H	272—274	4·43	226	2·54	Cl	H	276	4·48	230	3·11
H	Cl	268—270	4·41	230	3·30	H	Cl	270	4·28	232—234	3·43
Br	H	276	4·46	225	2·97	Br	H	280	4·45	230	3·27
H	Br	268—271	4·25	236	3·40	H	Br	270	4·19	238	3·35
I	H	278	5·53	230—232	4·33	I	H	280	4·40	236—240	3·32
H	I	234—235	4·46	246	4·01	H	I	234—236	4·40	248	4·07
		270—272	4·48					272—274	4·44		
Cl	Cl	276	4·51	234	3·34	Cl	Cl	276—278	4·46	234—238	3·58
Br	Cl	274	4·24	236	2·67	Br	Cl	276	4·57	238	3·27
						Cl	Br	276	4·52	238—240	3·37
Br	Br	272	4·52	238	3·59	Br	Br	280	4·49	240	3·42
Cl	Me	274—276	4·31	230	2·67	Cl	CO_2H	266—268	4·53	242—244	3·96
Br	Me	274—276	4·49	230—232	3·09	Br	CO_2H	260—264	4·39	226—228	3·92

FACULTY OF SCIENCE, ALEXANDRIA UNIVERSITY,
ALEXANDRIA, EGYPT, U.A.R.

[*Received, December 30th,* 1960.]

[7] Ljubawin, *Ber.*, 1877, **10**, 1366.
[8] Harries and Temme, *Ber.*, 1907, **40**, 165.

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568. *The Heat of Autoprotolysis of Sulphuric Acid.*

By B. Dacre and P. A. H. Wyatt.

In the molality range 0·06—0·09 the heat of the strong acid–strong base reaction

$$HB(HSO_4)_4(m) + 2KHSO_4(2\ molal) \longrightarrow KB(HSO_4)_4(m) + KHSO_4(m) + 2H_2SO_4$$

in sulphuric acid solution is found to be $-5{\cdot}60 \pm 0{\cdot}04$ kcal. mole^{-1} at 25°. Corrections are considered for the calculation from this of the heat of autoprotolysis of the solvent, which is judged to be about 5 kcal. mole^{-1}, in satisfactory agreement with the earlier thermal estimate.[1] Values obtained by other methods are discussed.

The existing estimates of ΔH_{ap}, the heat of autoprotolysis of sulphuric acid, depend to varying extents upon assumptions made in the interpretation of the properties of the pure acid. There has been only one thermal determination of this quantity [1] and, since this has inspired little confidence [2,3] and has recently been criticized,[4] a discussion of the relative merits of the suggested values of ΔH_{ap} is called for. Calculations made upon the temperature dependence of the autoprotolysis constant, K_{ap}, will obviously need revision whenever the detailed interpretation of the constitution of the pure acid is revised: this is illustrated by the values (in kcal. mole^{-1}) 2 (ref. 5), (× 2, refs. 1, 4? but see ref. 3), 6·1 (ref. 3), and 3·4 (ref. 4), which have been derived from time to time in this way. The attraction of this type of calculation probably lies in the understandable conviction that because cryoscopic and conductance measurements are more precise near the pure acid composition than thermal measurements, final values of equilibrium constants should be based upon them. It would be inadvisable to suppose however that the latest detailed calculations made by Gillespie and his co-workers [4,6] are yet sufficiently acceptable to justify rejection of the only thermal estimate of ΔH_{ap} as 40% too high. (Kirkbride and Wyatt [1] obtained $\Delta H_{ap} = 4{\cdot}8 \pm 0{\cdot}2$ kcal. mole^{-1}.) In particular, some doubt remains about the conductance treatment [7] and the description of dilute oleums.[8]

The principal assumption affecting the thermal determination [1] is that the concentrations of the autoprotolytic ions, $H_3SO_4^+$ and HSO_4^-, are equal in the pure solvent. Although an algebraic method was used in which ΔH_{ap} and K_{ap} were determined together, the actual value of $\Delta H_{ap}/2$ (subject to this assumption) was determined within fairly narrow limits by the difference between the partial molar heat content of a metal hydrogen sulphate in the pure solvent and at a concentration of HSO_4^- great enough for effective suppression of the autoprotolysis. If it is established [6] that $m_{HSO_4^-}$ exceeds $m_{H_3SO_4^+}$ significantly in the pure acid, this calculation will require modification. However, the criticism by Gillespie, Robinson, and Solomons [4] placed the emphasis differently and could be misleading. They conclude that because some of the differences in the recorded relative $\overline{L}_2$ values (see ref. 1, Table 7) may be due to non-ideality,[1] neither K_{ap} nor ΔH_{ap} determined in this way need be taken seriously. But non-ideal $\overline{L}_2$ contributions large enough to affect these calculations would of course be reflected in the temperature dependence of activity coefficients and cast doubt upon the validity of simple calculations [6] at any temperature. The thermal values of ΔH_{ap} and K_{ap} are also stated [4] to be "inconsistent with the position of minimum conductivity," but this is an overstatement since these values are actually only inconsistent with a particular conductance interpretation, which is itself open to some criticism.[7]

[1] Kirkbride and Wyatt, *Trans. Faraday Soc.*, 1958, **54**, 483.
[2] Gillespie and Robinson, *Adv. Inorgan. Radiochem.*, 1959, p. 385.
[3] Greenwood and Thompson, *J.*, 1959, 3474.
[4] Gillespie, Robinson, and Solomons, *J.*, 1960, 4320.
[5] Gillespie and Wasif, *J.*, 1953, 964.
[6] Bass, Gillespie, and Robinson, *J.*, 1960, 821.
[7] Wyatt, *Trans. Faraday Soc.*, 1961, **57**, 773.
[8] Dacre and Wyatt, to be published.

In view of these uncertainties, we have devised a new thermal experiment, the results of which will lead to a more direct estimate of ΔH_{ap} through assumptions of a different kind. In principle it resembles the determination of ΔH_{ap} for water by a simple strong acid–strong base neutralization, but it is slightly complicated by a method for overcoming corrections due to the solvent autoprotolysis. In precise thermochemical terms, the heat of the following reaction is measured at 25° and expressed per mole of $HB(HSO_4)_4$:

$$HB(HSO_4)_4(m) + 2KHSO_4(2\ molal) \longrightarrow KB(HSO_4)_4(m) + KHSO_4(m) + 2H_2SO_4 \quad . \quad . \quad . \quad (1)$$

$HB(HSO_4)_4$ being a strong acid [9] and $KHSO_4$ a strong base,[10] which is added to the acid in the form of a 2-molal solution in sulphuric acid. If only one equiv. of potassium hydrogen sulphate were added the reaction

$$H_2SO_4^+ + HSO_4^- \longrightarrow 2H_2SO_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

would not proceed to completion because of the solvent autoprotolysis in the " neutral " solution. The point of adding 2 equiv. is that the extent of solvent autoprotolysis should be approximately the same at the end of the experiment as at the beginning, so that complications due to the solvent autoprotolysis are eliminated. (If it transpires that the extent of autoprotolysis is not quite the same [6] at the same molality of strong acid and strong base, a slight correction can be made by interpolating to the base concentration at which the solvent effects are truly eliminated.)

Three determinations of ΔH for reaction (1) at different values of m (0·0630, 0·0825, 0·0901) gave a mean value of −5·60 kcal. per mole of $HB(HSO_4)_4$. To convert this precise experimental value to $-\Delta H_{ap}$, three corrections must be considered:

(i) The acid $HB(HSO_4)_4$ may not be completely strong.[2,11] For this reason the molality was kept within the cryoscopic range,[9] although higher molalities would have reduced still further the importance of autoprotolytic effects. In this range cryoscopy shows that there can be no appreciable proportion of the acid un-ionized, so that any correction for this effect must be small. A similar assumption has been made in conductance work.[12]

(ii) A correction is necessary for (twice) that part of the heat of dilution of 2-molal potassium hydrogen sulphate which is not accounted for by the suppression of solvent autoprotolysis. According to ref. 1, this would be $-2 \times H_A = -2 \times 0{\cdot}1$ kcal. mole^{-1}; but some uncertainty arises from the fact that the new $\overline{H}_2$ values for the addition of potassium hydrogen sulphate to the " neutral " $KB(HSO_4)_4$ solution are rather greater than those for additions to the pure acid.[1] (This may expose a slight systematic error between the two investigations, possibly traceable to an uncertainty in fixing the composition of the pure acid. The $\overline{L}_2$ values relative to the " neutral " solvent, however, agree satisfactorily with those in Table 7 of ref. 1.) We conclude that the appropriate correction will probably not exceed $\pm 0{\cdot}2$ kcal. mole^{-1}.

(iii) The most important correction is that for solvolysis of the $H_3SO_4^+$ ion in the strong-acid solution,[9] although precise calculation here depends upon the theory adopted for dilute oleums. Our present view is that Gillespie and his co-workers have overestimated the concentration of un-ionized $H_2S_2O_7$ in the dilute oleum region and that this is the principal cause of the discrepancies in interpretation which have arisen. Calculations are still in progress and we merely record here that the correction in question will probably not exceed 0·6 kcal. mole^{-1}. In terms of the interpretation by Gillespie and his co-workers [4] on the other hand, the correction is completely calculable. We have merely to add to the heat of reaction (1) a fraction of the heat of the reaction

$$H_2SO_4^+ + H_2SO_4 \rightleftharpoons H_3O^+ + H_2S_2O_7 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

demanded by the equilibrium constant $K_{id}/K_a = 4{\cdot}2 \times 10^{-5}/0{\cdot}014$, *i.e.* 0·003 mole kg.$^{-1}$.

[9] Flowers, Gillespie, and Oubridge, *J.*, 1956, 1925.
[10] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1933, **55**, 1900.
[11] Flowers, Gillespie, and Robinson, *Canad. J. Chem.*, 1960, **38**, 1363.
[12] Flowers, Gillespie, Robinson, and Solomons, *J.*, 1960, 4327.

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The heat of reaction (3) is $\Delta H_{id} - \Delta H_a$, *i.e.* 3·6 kcal. mole^{-1}, in their terms. The corrections become +0·6 to 0·7 kcal. mole^{-1}, depending upon the initial concentration of acid, so that in this way $\Delta H_{ap} = 5{\cdot}0 \pm 0{\cdot}2$ kcal. mole^{-1} would be calculated.

Confirmation that ΔH_{ap} must have approximately this value is also provided by the heat evolved per mole of HSO_4^- in the first additions to the acid. Thus, in the detailed example quoted in the experimental section, the first addition yields 4·98 kcal. mole^{-1}, but this requires correction for changes in the extents of autoprotolysis (+0·5 kcal. mole^{-1}) and $H_3SO_4^+$ solvolysis (*ca.* −0·1 kcal. mole^{-1}?) to give ΔH_{ap} (*ca.* 5·4 kcal. mole^{-1}).

Although the correction terms are clearly subject to revision, we conclude that the heat of reaction (1) provides a good guide to the magnitude of ΔH_{ap}, which must be approximately 5 kcal. mole^{-1}, within a few tenths of a kcal. mole^{-1}.

Experimental

The technique and apparatus for the thermal measurements have been described:[1] two Dewar flasks serve as twin calorimeters, one of which accommodates the reference junctions of the 20-junction copper–constantan thermel used for measuring the temperature changes. Into the main calorimeter were weighed about 1300 g. of a solution of known strength of tetra(hydrogen sulphato)boric acid[9] in pure sulphuric acid. This was prepared by adding a weight of boric acid required to remove the (cryoscopically determined) excess of disulphuric acid in a dilute oleum according to the stoicheiometric equation

$$H_3BO_3 + 3H_2S_2O_7 \longrightarrow H_3SO_4^+ + B(HSO_4)_4^- + H_2SO_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Although the total heat of reaction (1) was principally required, the reaction was actually carried out in stages since the intermediate readings of $\overline{H}_2$ for HSO_4^- additions were also of interest. Details of the set of measurements for one experiment are given in the Table. In this case 1 g. of the added base solution contained $1{\cdot}640 \times 10^{-3}$ mole of potassium hydrogen

Details of calculation for experiment 3.

HSO_4^- added (moles)	Moles (stoich.) ($H_3SO_4^+$)	Total H_2SO_4 (g.)	Heat evolved on addition (cal.)	Molality (stoich.) ($H_3SO_4^+$)	Mean molality during addn. ($H_3SO_4^+$)	$-\overline{H}_2$ rel. to 2m-$KHSO_4$ (kcal. mole^{-1})
—	0·1233	1369·3		0·0901		
			173·3		0·0769	4·98
0·0348	0·0885	1392·6		0·0636		
			164·2		0·0507	4·68
0·0351	0·0534	1416·7		0·0377		
			148·3		0·0255	4·33
0·0342	0·0192	1439·0		0·0133		
	(HSO_4^-)		100·5	(HSO_4^-)	0·0015	2·94
0·0342	0·0150	1458·9		0·0103	(HSO_4^-)	
			48·4		0·0195	1·78
0·0272	0·0422	1471·8		0·0287		
			25·8		0·0366	1·09
0·0236	0·0658	1482·0		0·0444		
			15·4		0·0517	0·69
0·0223	0·0881	1493·6		0·0590		
			9·7		0·0701	0·28
0·0346	0·1227	1510·2		0·0812		
			4·5		0·0919	0·13
0·0337	0·1564	1526·3		0·1025		

Total heat evolved up to addition of 2 × 0·1233 mole of HSO_4^- = 685·7 cal., whence $\Delta H(1) = -685{\cdot}7/0{\cdot}1233 = -5{\cdot}56$ kcal. mole^{-1}.

sulphate. For each addition the value of $\overline{H}_2$, the partial molar heat content of potassium hydrogen sulphate relative to a 2-molal solution, is also recorded. Apart from the reference already made to this quantity, we note that this type of experiment permits $\partial\overline{H}_2/\partial m_2$ at zero (stoicheiometric) concentration of HSO_4^- to be estimated with greater confidence than is possible with additions to the pure solvent, where negative concentrations of HSO_4^- are not

available.[13] The value of $(\partial\overline{H}_2/\partial m_2)_0$ for HSO_4^-, obtained graphically from the present result, is 65 kcal. mole^{-2} kg. ± 10%.

The three results for the overall heat of reaction (1) at 25° were: at initial H_2SO_4,$B(HSO_4)_4$ molality 0·0630, $\Delta H = -5{\cdot}59$ kcal. mole^{-1}; at 0·0825, $\Delta H = -5{\cdot}64$; at 0·0901, $\Delta H = -5{\cdot}56$. The mean value over the range 0·06—0·09 molal is therefore $-5{\cdot}60 \pm 0{\cdot}04$ kcal. mole^{-1}.

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THE UNIVERSITY, SHEFFIELD, 10. [*Received, January 24th*, 1961.]

[13] Wyatt, *Trans. Faraday Soc.*, 1956, **52**, 806.

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569. *Benzocyclobutenes. Part I. Attempted Syntheses of 1,2-Diphenylbenzocyclobutene.*

By WILSON BAKER, J. F. W. MCOMIE, G. A. POPE, and (in part) D. R. PRESTON.

o-Dibenzoylbenzene has been used as the starting point in attempted syntheses of 1,2-diphenylbenzocyclobutene (I). Pinacol reduction led to 1,3-diphenylisobenzofuran (VI), the *meso*- and racemic diols (IV), and 9,9′,10,10′-tetrahydro-10,10′-diphenyl-9,9′-bianthryl. The more accessible of the diols could not be converted into the related dibromo-derivative (XI); instead, cyclisation occurred to give 9-phenylanthracene. The diketone (V) was reduced with sodium in propan-2-ol to *o*-dibenzylbenzene (IX), which with *N*-bromosuccinimide gave either the α-bromo- or the αα′-dibromo-derivative (XI). Neither of these bromo-derivatives could be cyclised to benzocyclobutenes; instead they readily yielded derivatives of 9-phenylanthracene.

DERIVATIVES of benzocyclobutene were first made by Finkelstein [1] in 1910 and the parent compound was prepared by Cava and Napier [2] in 1956. So far all attempts to prepare benzocyclobutadiene or its derivatives have failed, although the transient existence of benzocyclobutadiene has been demonstrated by the formation of dimers [1,3] of this compound when attempting to prepare it, and also by trapping the benzocyclobutadiene with cyclopentadiene [4] and with furan.[5] The objectives of the experiments now described were the preparation of 1,2-diphenylbenzocyclobutene (I) and of the related butadiene in the hope that the latter might be stabilised by conjugation and be prevented from polymerising by steric hindrance. The experiments described in the present paper were not successful, but in retrospect this is not surprising since 1,2-diphenylbenzocyclobutene [6,7] is now known to be highly reactive and probably would not have survived under many of the experimental conditions which were used.

o-Dibenzoylbenzene (V), which was required for the present work, is not readily prepared by any of the previously described methods.[8] The most convenient starting-point for its preparation was 9,10-dihydro-9,10-dihydroxy-9,10-diphenylanthracene, prepared from anthraquinone and phenyl-lithium,[9] and this gave a high yield of *o*-dibenzoylbenzene (V) when oxidised with chromium trioxide. An attempt was made to reduce the diketone

[1] Finkelstein, *Ber.*, 1910, **43**, 1530; *Chem. Ber.*, 1959, **92**, xxxvii.
[2] Cava and Napier, *J. Amer. Chem. Soc.*, 1956, **78**, 500; 1958, **80**, 2255.
[3] Cava and Napier, *J. Amer. Chem. Soc.*, 1957, **79**, 1701.
[4] Nenitzescu, Avram, and Dinu, *Chem. Ber.*, 1957, **90**, 2541.
[5] Cava and Mitchell, *J. Amer. Chem. Soc.*, 1959, **81**, 5409.
[6] Jensen and Coleman, *J. Amer. Chem. Soc.*, 1958, **80**, 6149.
[7] Baker, McOmie, and Preston, *Chem. and Ind.*, 1960, 1305; Part II, following paper.
[8] Adams and Gold, *J. Amer. Chem. Soc.*, 1940, **62**, 56, and earlier references given there.
[9] Willemart, *Bull. Soc. chim. France*, 1942, **9**, 83.

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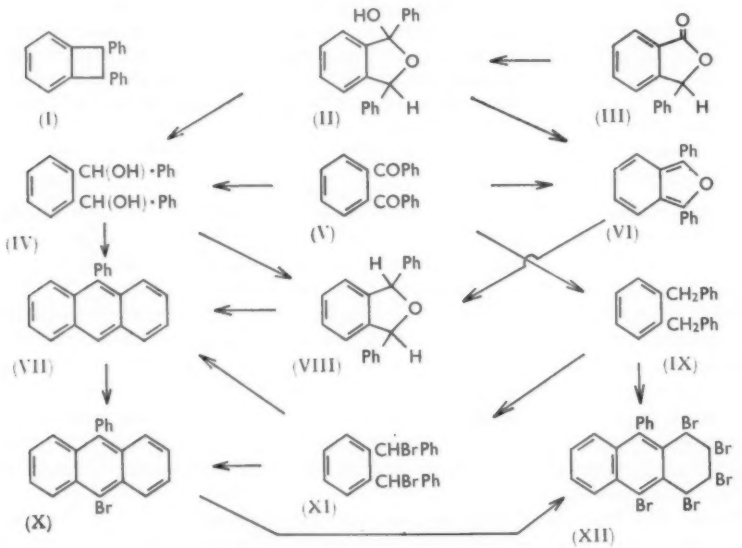
(V) to *o*-dibenzylbenzene (IX) by the modification of the Wolff–Kishner reduction introduced by Barton, Ives, and Thomas,[10] but the product was, not unexpectedly, 1,4-diphenylphthalazine.[11]

Clemmensen reduction of *o*-dibenzoylbenzene to *o*-dibenzylbenzene was unsuccessful, the diketone being unchanged even when we used the modification introduced by Martin,[12] which is particularly successful with sterically hindered ketones. Direct catalytic reduction of *o*-dibenzoylbenzene also proved difficult, and even under somewhat severe conditions the yield of *o*-dibenzylbenzene was only 23%. The most satisfactory procedure was found to be reduction with sodium in boiling isopentan-1-ol which gave *o*-dibenzylbenzene in 60% yield; the substance was apparently identical with that prepared in traces in a quite different manner by Huston and Friedmann.[13]

Reduction of *o*-dibenzoylbenzene with lithium aluminium hydride gave one of the two stereoisomeric forms (*meso* or racemic) of αα′-dihydroxy-*o*-dibenzylbenzene (IV), m. p. 127—128°, which is here designated as the α-form. A further route to the same diol started from 3-phenylphthalide (III), which when treated with phenylmagnesium bromide and then with aqueous ammonium chloride gave a good yield of 1-hydroxy-1,3-diphenylphthalan (II); the previously [11] described preparation of the phthalan (II) involved decomposition of the intermediate magnesium derivative with dilute mineral acid, causing dehydration to give 1,3-diphenylisobenzofuran (VI) as the major product. Reduction of the hydroxydiphenylphthalan (II) with sodium amalgam gave the α-diol (IV).



When attempting to replace the hydroxyl groups of the diol (IV) by bromine, it was found that the diol shows a remarkable tendency to undergo cyclodehydration to 9-phenylanthracene (VII), for example when treated with phosphorus tribromide and then with water (this paper); a similar dehydration occurs with sulphuric acid.[11] Again, 1,3-diphenylphthalan (VIII), prepared either by dehydration of the diol (IV) with hydrochloric acid or by reduction of 1,3-diphenylisobenzofuran (VI) with sodium amalgam,[11] also yields

[10] Barton, Ives, and Thomas, *J.*, 1955, 2056.
[11] Guyot and Catel, *Bull. Soc. chim. France*, 1906, **35**, 1124, 1135.
[12] Martin, *J. Amer. Chem. Soc.*, 1936, **58**, 1438.
[13] Huston and Friedmann, *J. Amer. Chem. Soc.*, 1916, **38**, 2527.

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9-phenylanthracene when boiled with hydrobromic acid (this paper), rather than giving αα′-dibromo-*o*-dibenzylbenzene (XI).

Several attempts to effect a pinacol reduction of 1,2-dibenzoylbenzene (V) to 1,2-dihydroxy-1,2-diphenylbenzocyclobutene were unsuccessful. Reduction with aluminium amalgam in benzene–ethanol or in aqueous ethanol (cf. ref.14) gave 1,3-diphenylisobenzofuran (VI), and the same product was obtained by reduction with sodium amalgam, with sodium in ether,[15] or with magnesium–magnesium iodide.[16] Reduction of *o*-dibenzoylbenzene with sodium amalgam in ethanol yielded the second stereoisomeric, β-form of αα′-dihydroxy-*o*-dibenzylbenzene (IV), m. p. 105—106°, which with acetic anhydride yielded the same diacetyl derivative as had been similarly prepared from the α-form of the diol; a geometrical rearrangement must be involved in one of these acetylations. A similar reduction in propanol–acetic acid gave the α-form of the diol (IV). Attempted pinacol reduction with zinc dust and alkali [17] again yielded the β-form of the diol (IV) and, curiously, a small quantity of anthraquinone. Treatment of *o*-dibenzoylbenzene with zinc dust in acetic acid was found by Boyd and Ladhams [18] and by Adams and Gold [8] to give 1,3-diphenylisobenzofuran (VI), whereas in boiling acetic acid (under which conditions pinacols are known to have been produced [19]) reduction proceeds further to give 9,9′,10,10′-tetrahydro-10,10′-diphenyl-9,9′-bianthryl.

In view of the failures to effect either a pinacol reduction of *o*-dibenzoylbenzene or conversion of the diol (IV) into a related dihalogen compound, the required αα′-dibromo-*o*-dibenzylbenzene (XI) was prepared by treatment of *o*-dibenzylbenzene (IX) with two equivalents of *N*-bromosuccinimide in carbon tetrachloride. When one equivalent of *N*-bromosuccinimide was used the monobromo-derivative of *o*-dibenzylbenzene was obtained. When *o*-dibenzylbenzene in carbon tetrachloride was boiled with an excess of brominating agent the product was 1,2,3,4,9-pentabromo-1,2,3,4-tetrahydro-10-phenylanthracene (XII), a compound which was also obtained by the addition of bromine to 9-bromo-10-phenylanthracene (X).

The dibromo-compound (XI) resembles other compounds in this series in its ready conversion into 9-phenylanthracenes on attempted cyclisation to a benzocyclobutene derivative. (*a*) When treated with sodium in ether under high-dilution conditions [20] it yielded 9-phenylanthracene (VII) and 10,10′-diphenyl-9,9′-bianthryl.[21] (*b*) With zinc dust and ethanol the product was the known adduct of 9-phenylanthracene and 9,10-dihydro-9-phenylanthracene.[22] (*c*) With potassium t-butoxide it yielded 9-bromo-10-phenylanthracene (X). (*d*) With sodium iodide in ethanol or acetone at temperatures from −80° to reflux temperature the products were 9-phenylanthracene, 9-bromo-10-phenylanthracene, and 9,9′,10,10′-tetrahydro-10,10′-diphenyl-9,9′-bianthryl.[23] Similarly, the reaction of α-bromo-*o*-dibenzylbenzene with ethanolic potassium hydroxide or t-butanolic potassium t-butoxide gave 9-phenylanthracene and the corresponding dihydro-compound as the only isolable products when the reaction was carried out at temperatures from 0° to reflux.

After the completion of this work, Jensen and Coleman [6] reported that they had prepared 1,2-diphenylbenzocyclobutene (I) by the action of sodium iodide on αα′-dibromo-*o*-dibenzylbenzene (XI) and by the action of bases on α-bromo-*o*-dibenzylbenzene, but no experimental details were given of these reactions or of the preparation of the bromo-compounds. In a subsequent communication [24] Jensen described the preparation of *o*-dibenzylbenzene (IX)

[14] Newman, *J. Amer. Chem. Soc.*, 1940, **62**, 1683; Lloyd and Rowe, *J.*, 1954, 4232.
[15] Bachmann, *J. Amer. Chem. Soc.*, 1933, **55**, 1179.
[16] Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1927, **49**, 236.
[17] Baker and McGowan, *J.*, 1937, 559.
[18] Boyd and Ladhams, *J.*, 1928, 2089.
[19] Pauson, *J. Amer. Chem. Soc.*, 1954, **76**, 2187.
[20] Cope and Fenton, *J. Amer. Chem. Soc.*, 1951, **73**, 1668.
[21] Barnett and Cook, *J.*, 1923, **123**, 2639.
[22] Haack, *Ber.*, 1929, **62**, 1771.
[23] Schlenk and Bergmann, *Annalen*, 1928, **464**, 40.
[24] Jensen, *J. Org. Chem.*, 1960, **25**, 269.

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by catalytic reduction of *o*-dibenzoylbenzene, itself made in 32% yield by the action of phenylmagnesium bromide on phthaloyl chloride at −55°. More recently, Cava, Mitchell, and Deana [25] tried to prepare compound (I) by pyrolysis of 1,3-diphenyl-2-thiaindane 2,2-dioxide, but they obtained only 9-phenylanthracene. Likewise, dehydrogenation and decarboxylation of 7,8-diphenylbicyclo[4,2,0]oct-6-ene-3,4-dicarboxylic acid gave, not the benzocyclobutene (I), but a mixture of 9-phenylanthracene and *o*-dibenzylbenzene.[26] A synthesis of the benzocyclobutene (I) has, however, been achieved [7] from 1,3-dihydro-1,3-diphenylisoindole and is fully described in the following paper.

Experimental

o-*Dibenzoylbenzene* (V).—9,10-Dihydro-9,10-dihydroxy-9,10-diphenylanthracene [9] (10·9 g.) in glacial acetic acid (75 ml.) was oxidised by addition during ½ hr. of a solution of chromium trioxide (30 g.) in acetic acid (150 ml.) and water (50 ml.) at 70° with constant stirring. After being heated for a further 2 hr. on the steam-bath, the cooled mixture was poured into water, and the product was collected, washed with water and with dilute alkali, and crystallised from ethanol, giving *o*-dibenzoylbenzene as colourless rhombs, m. p. 145—146° (6·8 g., 79%) (lit.,[11] m. p. 146°). The *mono-2,4-dinitrophenylhydrazone*, prepared in ethanol–hydrochloric acid solution, separated from ethanol in rhombic prisms, m. p. 199—200° (Found: C, 66·8; H, 3·9; N, 12·3. $C_{26}H_{18}N_4O_5$ requires C, 66·9; H, 3·8; N, 12·0%).

o-*Dibenzylbenzene* (IX).—(*a*) *o*-Dibenzoylbenzene (2·0 g.) in ethanol (120 ml.) was shaken at 70° for 12 hr. in hydrogen at 23 atm. pressure in presence of 10% palladium–charcoal. The filtered solution was evaporated, and the residue extracted with ether (the diketone is sparingly soluble), giving *o*-dibenzylbenzene which separated from ethanol in thin prisms, m. p. 77—78° (0·43 g.) (Found: C, 93·0; H, 7·1. Calc. for $C_{20}H_{18}$: C, 93·0; H, 7·0%). Huston and Friedemann [13] give m. p. 78°.

(*b*) *o*-Dibenzoylbenzene (2·0 g.) dissolved in isopentan-1-ol (200 ml.; redistilled) was added at the b. p. to small pieces of sodium (20 g.) with vigorous stirring. When the reaction had subsided a further volume of isopentanol was added; when all sodium had reacted, the solvent was removed in steam, and the residual oil which solidified was crystallised twice from ethanol, giving *o*-dibenzylbenzene, m. p. 77—78° (1·1 g.).

αα′-*Dihydroxy*-o-*dibenzylbenzene* (IV) (α-*Form*).—(a) *By reduction of* o-*dibenzoylbenzene*. *o*-Dibenzoylbenzene (2·8 g.) was added by extraction from a Soxhlet thimble, to a refluxing solution of lithium aluminium hydride (2·2 g.) in anhydrous ether (200 ml.), and after treatment with dilute sulphuric acid the ethereal layer yielded a yellow oil (2·7 g.). This product was adsorbed on a column of alumina and eluted with benzene; of the two bands detected in ultraviolet light the upper yielded a solid which was crystallised twice from 50% methanol–water, giving αα′-dihydroxy-*o*-dibenzylbenzene (IV) as rhombs, m. p. 127—128° (α-form) (1·3 g., 45%). The m. p. was undepressed on admixture with a specimen of the diol prepared as described by Guyot and Catel.[11] The *diacetyl derivative* of (IV), prepared by reaction with acetic anhydride at 100° and crystallised from ethanol, had m. p. 107—108° (Found: C, 76·9; H, 6·1. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9%).

(b) *By reduction of* 1-*hydroxy*-1,3-*diphenylphthalan*. A solution of the phthalan [11] (11·5 g.) in methanol (130 ml.) was boiled for 6 hr. with 2% sodium amalgam (100 g.), and the residue left on evaporation of the solvent was crystallised from methanol–water (1 : 1). The dihydroxy-compound separated in rhombs (8·5 g.), m. p. 127—128°.

9-*Phenylanthracene* (VII).—(a) *From* 1,3-*diphenylphthalan*. 1,3-Diphenylphthalan [11] (5·4 g.) was boiled under reflux for 5 hr. with 48% aqueous hydrogen bromide (10 ml.). Neutralisation with sodium carbonate and extraction with ether gave 9-phenylanthracene which separated from ethanol as pale green leaflets, m. p. 153—154° (2·5 g.; 48%) (lit.,[27] m. p. 152—153°).

(b) *From* αα′-*dihydroxy*-o-*dibenzylbenzene*. The diol (IV) (1·0 g.; m. p. 127—128°) in benzene (75 ml.) containing a few drops of pyridine was treated dropwise at 70° with phosphorus tribromide (1·6 ml.) and then kept at 55° for 2 hr. After treatment with aqueous alkali the benzene solution yielded 9-phenylanthracene, m. p. 153—154° (0·49 g., 57%) after crystallisation from ethanol.

[25] Cava, Mitchell, and Deana, *J. Org. Chem.*, 1960, **25**, 1481.
[26] Blomquist and Meinwald, *J. Amer. Chem. Soc.*, 1960, **82**, 3619.
[27] Baeyer and Schillinger, *Annalen*, 1880, **202**, 61.

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Reduction of o-*Dibenzoylbenzene* (V). *Formation of* 1,3-*Diphenylisobenzofuran* (VI).—(a) *With aluminium amalgam.* Aluminium foil (12 g.; previously etched with 10% aqueous sodium hydroxide, washed, and dried) and mercuric chloride (0·5 g.) were added to *o*-dibenzoylbenzene (8·6 g.) in benzene (200 ml.) and absolute ethanol (300 ml.). Reaction was initiated by warming and, when it had subsided, the mixture was heated on the water-bath for 6 hr. and poured into dilute hydrochloric acid. The benzene layer yielded a solid which was crystallised from light petroleum (b. p. 60—80°) giving 1,3-diphenylisobenzofuran as thin yellow plates, m. p. 124—125° (lit.,[11] m. p. 125°) (5·5 g., 68%) (Found: C, 89·2; H, 5·3. Calc. for $C_{20}H_{14}O$: C, 88·9; H, 5·2%).

(b) *With sodium amalgam in ether.* *o*-Dibenzoylbenzene (5·7 g.) in anhydrous ether (200 ml.) was shaken for 100 hr. with 2% sodium amalgam (50 g.) under nitrogen, and the mixture added to 10% acetic acid (400 ml.), also under nitrogen. The ethereal layer yielded a colourless powder which slowly became yellow, and after crystallisation from light petroleum gave 1,3-diphenylisobenzofuran, m. p. 124—125° (3·0 g., 56%). A similar experiment with an excess of sodium wire in place of the sodium amalgam gave 1,3-diphenylisobenzofuran in 42% yield.

(c) *With magnesium and magnesium iodide.* A solution of *o*-dibenzoylbenzene (3·0 g.) in benzene (50 ml.) was added slowly to a solution of magnesium and magnesium iodide in benzene–ether made according to Gomberg and Bachmann's directions [18] from magnesium (2 g.). After being boiled for 3 hr. the filtered benzene solution was washed with dilute hydrochloric acid, dried, and evaporated, and the residue was crystallised from light petroleum (b. p. 60—80°), purified by passage in benzene over alumina, and finally recrystallised from light petroleum, giving 1,3-diphenylisobenzofuran, m. p. 124—125° (1·8 g., 63%).

Reduction of o-*Dibenzoylbenzene with Sodium Amalgam.*—(a) *In ethanol. Formation of* αα′-*dihydroxy-o-dibenzylbenzene, m. p.* 105—106° (β-*form*). 2% Sodium amalgam (300 g.) was added during ½ hr. to a solution of *o*-dibenzoylbenzene (4·6 g.) in 95% ethanol (100 ml.). When the strongly exothermic reaction had ended the alcoholic solution was poured into water and extracted with ether from which an oil was obtained. Treatment with boiling aqueous ethanol yielded the β-*isomer* of αα′-dihydroxy-*o*-dibenzylbenzene as thin, colourless prisms, m. p. 105—106° (1·8 g., 39%) (Found: C, 83·2; H, 6·1. $C_{20}H_{18}O_2$ requires C, 82·8; H, 6·2%). The diacetyl derivative, prepared by heating it with acetic anhydride at 100° and crystallised from ethanol, had m. p. 107—108°, undepressed on admixture with the diacetyl derivative of the α-diol.

(b) *In propanol–acetic acid. Formation of* αα′-*dihydroxy-o-dibenzylbenzene, m. p.* 127—128°. The above reaction when repeated with *o*-dibenzoylbenzene (2·9 g.) in propanol (75 ml.) and acetic acid (75 ml.) and 2% sodium amalgam (200 g.) gave αα′-dihydroxy-*o*-dibenzylbenzene, m. p. 127—128° (1·2 g., 42%).

Reduction of o-*Dibenzoylbenzene with Zinc Dust.*—(a) *In alkali.* A mixture of *o*-dibenzoylbenzene (2·9 g.) in ethanol (50 ml.), zinc dust (20 g.) and 10% aqueous potassium hydroxide (20 ml.) was heated on the water-bath for 8 hr., filtered, concentrated to ½ volume, added to water, and extracted with ether. The product was crystallised from ethanol, giving pale yellow needles, m. p. 283—284° (0·3 g.) (Found: C, 80·6; H, 3·9. Calc. for $C_{14}H_8O_2$: C, 80·7; H, 3·9%). A mixed m. p. with anthraquinone showed no depression. The mother-liquors gave a product which crystallised from aqueous ethanol in prisms, m. p. 105—106° (1·6 g., 56%), undepressed on admixture with the previously prepared αα′-dihydroxy-*o*-dibenzylbenzene of the same m. p. The diacetyl derivative had m. p. 107—108°.

(b) *In acetic acid.* Zinc dust (60 g.) was added in portions during 15 min. to *o*-dibenzoylbenzene (11·5 g.) in boiling acetic acid (250 ml.). After being boiled for 3 hr. the hot solution was filtered and then poured into water (1 l.). Next day the solid was collected and recrystallised from ethanol, giving 9,9′,10,10′-tetrahydro-10,10′-diphenyl-9,9′-bianthryl (8·4 g.) as yellow prisms, m. p. 254—255·5° (lit.,[23] m. p. 260°). This compound is identical (mixed m. p., ultraviolet and infrared spectra) with that obtained by the action of sodium iodide on αα′-dibromo-*o*-dibenzylbenzene.

α-*Bromo-o-dibenzylbenzene.*—A mixture of *o*-dibenzylbenzene (1·0 g.), *N*-bromosuccinimide (0·69 g.), benzoyl peroxide (10 mg.), and carbon tetrachloride (15 ml.) was stirred at 40° for 3 hr. under illumination from a 200-w tungsten-filament lamp. More benzoyl peroxide (10 mg.) was added after the first 1·5 hr. The cooled solution was filtered and concentrated under reduced pressure. The residual yellow oil (1·33 g., 99%) consisted of essentially pure α-*bromo-o-dibenzylbenzene* (Found: C, 70·8; H, 5·1. $C_{20}H_{17}Br$ requires C, 71·1; H, 5·4%). It decomposed on attempted distillation.

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αα′-Dibromo-o-dibenzylbenzene (XI).—The preceding experiment was repeated with 2 equivalents of *N*-bromosuccinimide (*i.e.* 1·39 g.) and gave the *dibromo-compound* as a yellow oil (1·60 g., 96%) which did not crystallise and decomposed when heated above 40° (Found: C, 57·2; H, 3·8. $C_{20}H_{16}Br_2$ requires C, 57·7; H, 3·8%).

1,2,3,4,10-Pentabromo-1,2,3,4-tetrahydro-9-phenylanthracene (XII).—(a) *From o-dibenzylbenzene and N-bromosuccinimide.* *o*-Dibenzylbenzene (1·0 g.) in carbon tetrachloride (20 ml.) was boiled for 5 hr. with *N*-bromosuccinimide (3·44 g., 5 equiv.) and a trace of dibenzoyl peroxide, then cooled and filtered. The filtrate, on being shaken with aqueous sodium hydrogen sulphite and then evaporated, left a residue which after several crystallisations from acetone yielded the *pentabromo-derivative* as prisms, m. p. 160—161° (0·5 g.) (Found: C, 37·4; H, 2·3; Br, 60·3. $C_{20}H_{13}Br_5$ requires C, 36·8; H, 1·9; Br, 61·2%).

(b) *From 9-bromo-10-phenylanthracene* (X). A solution of the bromo-compound (X) (0·5 g.) and bromine (0·5 g.) in carbon tetrachloride (10 ml.) was boiled for 12 hr., and after evaporation the product was crystallised from acetone, giving the pentabromo-derivative, m. p. and mixed m. p. 160—161°.

Reaction of αα′-Dibromo-o-dibenzylbenzene with Sodium in Ether.—The experiment was carried out with carefully dried materials and a high-dilution apparatus.[20] The dibromo-compound (9·0 g.) in ether (200 ml.) was added during 12 hr. to a stirred boiling mixture of ether (200 ml.) and powdered sodium (4 g.); stirring and boiling were continued for a further 8 hr. The filtered solution was distilled, and the fraction of b. p. 194—200°/1 mm., which solidified, was recrystallised from ethanol, giving 9-phenylanthracene (VII) as pale green leaflets, m. p. 153—154° (1·4 g.) (Found: C, 94·5; H, 5·5. Calc. for $C_{20}H_{14}$: C, 94·5; H, 5·5%). The residual material from the distillation was extracted with boiling toluene, and the solution deposited 10,10′-diphenyl-9,9′-bianthryl as a faintly yellow powder (2·4 g.), m. p. >300° (lit.,[21] m. p. >300°) (Found: C, 95·1; H, 5·3. Calc. for $C_{40}H_{28}$: C, 94·9; H, 5·1%).

Reaction of αα′-Dibromo-o-dibenzylbenzene with Zinc and Ethanol.—The dibromo-compound (4·2 g.) in 95% ethanol (50 ml.) was added slowly to a boiling mixture of 95% ethanol (100 ml.) and zinc dust (1·3 g.), and boiling was continued for a further 4 hr. The filtered solution was concentrated, water added, and the whole extracted with ether. The extract yielded a product which solidified (2·5 g.) and was crystallised four times from ethanol, giving almost colourless needles, m. p. 119—120° (1·9 g.) (Found: C, 94·0; H, 6·1. Calc. for $C_{40}H_{30}$: C, 94·0; H, 6·0%). This substance appears to be a 1 : 1 adduct of 9-phenylanthracene and 9,10-dihydro-9-phenylanthracene which has been described by Haack [22] as having m. p. 119—120°.

Reaction of αα′-Dibromo-o-dibenzylbenzene with Potassium t-Butoxide. Formation of 9-Bromo-10-phenylanthracene (X).—The dibromo-compound (4·2 g.) was boiled with potassium t-butoxide in t-butyl alcohol (from potassium 0·46 g., and the alcohol 20 ml.) for 4 hr., then evaporated under diminished pressure, and the residue was treated with dilute acid and extracted with ether. The extract yielded a product which was twice crystallised from ethanol, giving 9-bromo-10-phenylanthracene (1·4 g.), m. p. and mixed m. p. with an authentic specimen 154—155° (lit.,[23] m. p. 154—155°).

Reaction of αα′-Dibromo-o-dibenzylbenzene with Sodium Iodide.—A mixture of the dibromo-compound (2·0 g.), sodium iodide (1·6 g., 2·2 equiv.), and ethanol was stirred at 40° for 12 hr. The cooled solution was filtered and dilute aqueous sodium thiosulphate was added to the filtrate until all the iodine had reacted. The resulting mixture yielded to ether a yellow oil which partly solidified. Recrystallisation from ethanol gave 9,9′,10,10′-tetrahydro-10,10-diphenyl-9,9′-bianthryl (0·45 g., 35%), m. p. 257—258°. The mother-liquor was evaporated and the residue, dissolved in benzene, was chromatographed on alumina, giving 9-bromo-10-phenylanthracene (0·16 g., 10%), m. p. and mixed m. p. 154—155° (from ethanol), and 9-phenylanthracene (0·20 g., 15%), m. p. and mixed m. p. 150—151° (from ethanol).

Similar results were obtained when the reaction was carried out at −80°, −40°, 0°, 20°, or reflux temperature and when acetone was used in place of ethanol as the solvent and the reaction was carried out at −80°, 0°, 20°, and reflux temperature.

Reaction of α-Bromo-o-dibenzylbenzene with Bases.—(a) *With potassium hydroxide.* A solution of the bromo-compound (1·06 g.) in ethanol (12 ml.) containing potassium hydroxide (0·27 g., 1·5 equiv.) was stirred at room temperature for 6 hr. The solution was then filtered and the solid was washed with water, leaving 9,9′,10,10′-tetrahydro-10,10′-diphenyl-9,9′-bianthryl (14 mg.), m. p. 220—235° (identified by its infrared spectrum: it had possibly originated from

[20] Cook, *J.*, 1926, 2168.

traces of dibromo-compound in the starting material). The ethanolic filtrate was diluted with water (50 ml.) and then extracted with ether. Distillation of the dried ethereal solution gave an oil (800 mg.; b. p. 110—120°/0·05 mm.) which partly solidified. Recrystallisation of the solid from ethanol gave the 1 : 1 adduct of 9-phenylanthracene and 9,10-dihydro-9-phenylanthracene (500 mg., 62%), m. p. and mixed m. p. 117—118°.

When the reaction was carried out at 0° or at the reflux temperature of ethanol similar results were obtained.

(b) *With potassium t-butoxide.* The bromo-compound (1·27 g.) in t-butyl alcohol (20 ml.) containing potassium t-butoxide (0·63 g., 1·5 equiv.) was stirred at 35° for 24 hr., then water (100 ml.) was added and the whole was extracted with ether. The extracts yielded a yellow oily solid which recrystallised from ethanol, giving the 1 : 1 adduct as above (550 mg., 57%), m. p. 117—118°. Chromatography on alumina of the mother-liquors in benzene gave 9,10-dihydro-9-phenylanthracene (85 mg., 9%), m. p. 85—86°, and 9-phenylanthracene (160 mg., 16·5%), m. p. 149—151°. The same products were obtained when the reaction was carried out for shorter times at these temperatures or at 80°.

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570. *Benzocyclobutenes. Part II.* A New Synthesis of Benzocyclobutene and of 1,2-Diphenylbenzocyclobutene.*

By WILSON BAKER, J. F. W. MCOMIE, and D. R. PRESTON.

Benzocyclobutene (II), accompanied by some 1,2:5,6-dibenzocyclooctadiene, is obtained when the N-toluene-*p*-sulphonamido-derivative of 1,3-dihydroisoindole (I) is treated with aqueous sodium hydroxide. Similarly 1,2-diphenylbenzocyclobutene (VIII) is formed by the spontaneous decomposition of 1,3-dihydro-1,3-diphenyl-*N*-toluene-*p*-sulphonamidoisoindole (VII) in pyridine solution.

BENZOCYCLOBUTENES have been prepared by five different methods, three of which are of general application; they are mentioned in a preliminary communication [1] reporting a new general synthesis now recorded in detail.

The oxidation of 1,1-dibenzylhydrazines, $(Ph{\cdot}CH_2)_2N{\cdot}NH_2$, with mercuric oxide to bibenzyl and nitrogen was first recorded by Busch and Weiss;[2] other oxidising agents have since been employed.[3] The closely related reaction due to Bamford and Stevens by which benzaldehyde benzenesulphonylhydrazone, $Ph{\cdot}CH{:}N{\cdot}NH{\cdot}SO_2Ph$, is converted into benzenesulphinic acid and phenyldiazomethane by treatment with alkali,[4] led Carpino to develop a process for the preparation of bibenzyls in which *NN*-dibenzylbenzene(or toluene-*p*-)sulphonylhydrazides are decomposed by alkali to give the bibenzyl, sodium benzene(or toluene-*p*-)sulphinate and nitrogen:[5]

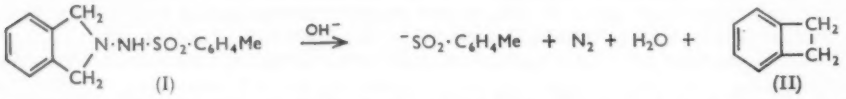
$$(Ph{\cdot}CH_2)_2N{\cdot}NH{\cdot}SO_2{\cdot}Ph \xrightarrow{OH^-} Ph{\cdot}CH_2{\cdot}CH_2Ph + N_2 + {}^-SO_2{\cdot}Ph + H_2O$$

This suggested that it should be possible to prepare benzocyclobutene (II), which is in a

* Part I, preceding paper.

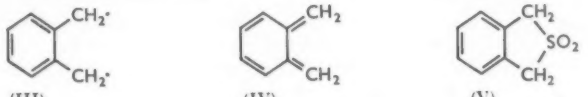
[1] Baker, McOmie, and Preston, *Chem. and Ind.*, 1960, 1305.
[2] Busch and Weiss, *Ber.*, 1900, **33**, 270.
[3] Overberger and Marks, *J. Amer. Chem. Soc.*, 1955, **77**, 4104.
[4] Bamford and Stevens, *J.*, 1952, 4335.
[5] Carpino, *Chem. and Ind.*, 1957, 172; *J. Amer. Chem. Soc.*, 1957, **79**, 4427.

sense a bibenzyl, by a similar reaction from the toluene-*p*-sulphonyl derivative of *N*-amino-1,3-dihydroisoindole (I):



(I) (II)

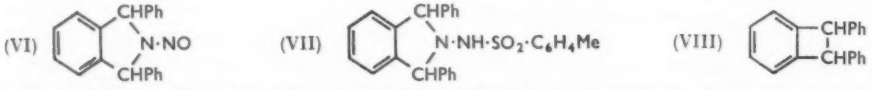
This expectation has been realised. The toluene-*p*-sulphonyl derivative (I) reacts with 20% aqueous sodium hydroxide at 70—80°, giving in a small-scale reaction a 16% yield of a hydrocarbon mixture, containing benzocyclobutene (II) and *o*-xylene in a ratio of about 10 : 1. The hydrocarbons were identified by their infrared spectra. Their relative proportions were established by observation of the infrared spectra and gas–liquid chromatographic behaviour of mixtures of the two pure substances, the benzocyclobutene required for purposes of comparison being prepared by the method of Cava and Napier.[6] A relatively non-volatile product isolated from the reaction mixture in 12% yield was proved to be 1,2:5,6-dibenzocyclo-octadiene.



(III) (IV) (V)

The reaction doubtless proceeds *via* the diradical (III), a canonical form of the dimethylene-*o*-quinone (IV), which then cyclises to benzocyclobutene (II), dimerises to 1,2:5,6-dibenzocyclo-octadiene, or combines with hydrogen to give *o*-xylene. The free-radical nature of the reaction is strongly indicated by the fact that the thermal decomposition of 2-thiaindane dioxide (V) likewise gives benzocyclobutene, *o*-xylene, and 1,2:5,6-dibenzocyclo-octadiene in almost the same proportions as now found.[7]

The reaction has been extended to the preparation of 1,2-diphenylbenzocyclobutene (VIII). 1,3-Dihydro-*N*-nitroso-1,3-diphenylisoindole (VI) was reduced with aluminium amalgam to the *N*-amino-compound which was isolated as the hydrochloride. When this hydrochloride was treated in pyridine with toluene-*p*-sulphonyl chloride 1,3-dihydro-1,3-diphenyl-*N*-toluene-*p*-sulphonamidoisoindole underwent spontaneous decomposition at room temperature to give a mixture, separated chromatographically, of 1,2-diphenylbenzocyclobutene (VIII), m. p. 93—94°, in about 40% yield, and 9,10-dihydro-9-phenylanthracene



in about 13% yield. The 1,2-diphenylbenzocyclobutene (VIII) had almost exactly the same m. p. and ultraviolet and infrared spectra as those recorded for the material prepared by treating αα′-dibromo-*o*-dibenzylbenzene with sodium iodide and described in a preliminary note by Jensen and Coleman.[8]

Experimental

1,3-*Dihydro*-N-*nitrosoisoindole*.—Toluene-*p*-sulphonamide and *o*-xylylene dibromide gave 1,3-dihydro-N-toluene-*p*-sulphonyl-isoindole,[9] which was hydrolysed by aqueous hydrobromic acid in propionic acid in presence of phenol to give 1,3-dihydroisoindole, characterised as its picrate,[9,10] m. p. 195—196·5° (Found: C, 48·9; H, 3·8; N, 16·1. Calc. for $C_8H_9N,C_6H_3N_3O_7$:

[6] Cava and Napier, *J. Amer. Chem. Soc.*, 1958, **80**, 2255.
[7] Cava and Deana, *J. Amer. Chem. Soc.*, 1959, **81**, 4266.
[8] Jensen and Coleman, *J. Amer. Chem. Soc.*, 1958, **80**, 6149.
[9] Bornstein, Lashua, and Boisselle, *J. Org. Chem.*, 1957, **22**, 1255.
[10] Fenton and Ingold, *J.*, 1928, 3295.

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C, 48·3; H, 3·5; N, 16·1%). The derived 1,3-dihydro-*N*-nitrosoisoindole [11] formed needles, m. p. 95—97°, from ethanol (lit.,[11] m. p. 96—97°).

2-Amino-1,3-dihydroisoindole.—1,3-Dihydro-*N*-nitrosoisoindole (1·37 g.) in dry ether (50 ml.) was stirred during the addition (1 hr.) at room temperature of lithium aluminium hydride (370 mg.; 1·05 equiv.) in ether (30 ml.). The mixture was shaken with damp ether (40 ml.) and then with 20% aqueous sodium hydroxide (40 ml.), the ethereal layer dried (K_2CO_3) and evaporated under reduced pressure and then distilled, giving 2-amino-1,3-dihydroisoindole as an almost colourless liquid (880 mg., 69%), b. p. 115—120°/24 mm., which rapidly darkened in air. The hydrochloride, precipitated from hot ethanolic solution by addition of ether, formed light grey needles, m. p. 189—195° (decomp.) (Found: N, 16·1. Calc. for $C_8H_{11}ClN_2$: N, 16·4%) (lit.,[12,5] m. p. 190—194° and 185—195°).

1,3-Dihydro-2-toluene-p-sulphonamidoisoindole (I).—The preceding hydrochloride (0·75 g.) in dry pyridine (4 ml.) was stirred at 0° during the addition (5 min.) of toluene-*p*-sulphonyl chloride (0·53 g.). After a further ¼ hr. at 0° water (20 ml.) was added and the solid collected, dissolved in hot acetone, and precipitated by the addition of water, giving light-brown needles (0·70 g., 56%), m. p. 130—135° (decomp.) (Carpino [5] prepared the compound in dimethylformamide and gives m. p. 136—138° for the pure compound).

Action of Alkali on 1,3-Dihydro-2-toluene-p-sulphonamidoisoindole. Isolation of Benzocyclobutene (II) *and 1,2:5,6-Dibenzocyclo-octadiene.*—The sulphonamido-derivative (I) (0·70 g.) was added in portions to 20% aqueous sodium hydroxide (5 ml.) at 70—80° (¼ hr.). When gas evolution had ceased the cooled solution was extracted with ether, and the extracts were washed with dilute hydrochloric acid, dried ($MgSO_4$), and distilled, giving a colourless oil (40 mg.), b. p. 95—102°/100 mm. The infrared spectrum of this oil showed peaks at 715 and 780 cm.$^{-1}$ (split band corresponding to four adjacent aromatic hydrogen atoms in benzocyclobutene [6]) and at 740 cm.$^{-1}$ (four adjacent aromatic hydrogen atoms in *o*-xylene). Comparison of the spectrum of the product with those of mixtures of the two compounds in known proportions indicated that the ratio of benzocyclobutene to *o*-xylene was approximately 10 : 1, and this was confirmed by gas–liquid chromatography of the product and of mixtures of the two compounds. If high temperatures and low flow rates were used on the column, benzocyclobutene tended to isomerise to a compound identified as styrene by comparison of its retention time with genuine material (cf. Cava and Deana [7]). Gas-chromatography was effected in an 8 ft. column, packed with 20% Apiezon L on Silocel C-22, at 250° with a flow rate of 40 ml. of nitrogen per min.

The residue from the distillations was sublimed several times at 100—120°/0·2 mm., giving 1,2:5,6-dibenzocyclo-octadiene (30 mg., 12%), m. p. 106—108°, mixed m. p. with an authentic specimen,[13] 107—108·5°.

1,3-Dihydro-2-nitroso-1,3-diphenylisoindole (VI).—To 1,3-dihydro-1,3-diphenylisoindole [14] (4·7 g.) in water (200 ml.) and concentrated sulphuric acid (1·3 ml.) was added during 20 min. with ice-cooling, sodium nitrite (1·45 g.) in water (10 ml.), and the mixture was stirred for a further 3 hr. The solid was washed, dried, and crystallised from ethanol, giving 1,3-dihydro-2-nitroso-1,3-diphenylisoindole (VI) (3·6 g., 70%) as colourless needles, m. p. 175·5—176·5° (lit.,[14] m. p. 175—175·5°) (Found: C, 80·3; H, 5·7; N, 9·6. Calc. for $C_{20}H_{16}N_2O$: C, 80·0; H, 5·4; N, 9·4%).

2-Amino-1,3-dihydro-1,3-diphenylisoindole.—Finely powdered 1,3-dihydro-2-nitroso-1,3-diphenylisoindole (VI) (300 mg.) was added during ¼ hr. to a stirred suspension of aluminium amalgam (from 1·0 g. of aluminium [15]) in ether (25 ml.), water (6·0 ml.) was then added dropwise during ½ hr., and stirring was continued for a further 1 hr. The ethereal suspension was then shaken with 10% aqueous sodium hydroxide (50 ml.), dried (K_2CO_3), and filtered, and anhydrous hydrogen chloride was passed through the solution. The precipitated *2-amino-1,3-dihydro-1,3-diphenylisoindole hydrochloride* (270 mg., 83%), crystallised from water, had m. p. 225—228° (decomp.) (Found: N, 8·9. $C_{20}H_{17}ClN_2$ requires N, 8·7%).

1,2-Diphenylbenzocyclobutene (VIII).—Finely divided toluene-*p*-sulphonyl chloride (200 mg., 1·0 equiv.) was added to 2-amino-1,3-dihydro-1,3-diphenylisoindole hydrochloride (270 mg.) in

[11] Gabriel and Neumann, *Ber.*, 1893, **26**, 527.
[12] Fränkel, *Ber.*, 1900, **33**, 2812.
[13] Baker, Banks, Lyon, and Mann, *J.*, 1945, 27.
[14] Boyd and Ladhams, *J.*, 1928, 2093.
[15] Vogel, *J.*, 1927, 594.

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pyridine (1·5 ml.) at room temperature. Slow evolution of nitrogen began at once, and, after it had ceased (6 hr.), the solution was boiled for ½ hr., poured into dilute hydrochloric acid, and extracted with ether (3 × 20 ml.). The extracts were shaken with aqueous sodium hydroxide to remove toluene-*p*-sulphinic acid, dried, and distilled, leaving a viscous, yellow oil (112 mg.), whose benzene solution was chromatographed on an alumina column. The final fraction (20 mg.) did not crystallise. The first fraction (77 mg.) solidified, and was crystallised from ethanol at 0°, giving 1,2-diphenylbenzocyclobutene (VIII) as colourless needles, m. p. 93—94°, $\lambda_{max.}$ at 261 (log ε 3·32), 266 (3·55), and 272·5 mμ (3·27); Jensen and Coleman [8] give m. p. 94·5—95·2° and $\lambda_{max.}$ 260 (log ε 3·24), 266 (3·36), and 272 mμ (3·32). The second fraction (22 mg.) also solidified and when crystallised from ethanol gave 9,10-dihydro-9-phenylanthracene, m. p. 85—86°.

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571. *Molecular Interaction: Molecular Polarisation of Amines in Benzene and Carbon Tetrachloride.*

By A. N. SHARPE and S. WALKER.

Evidence of weak interaction between amines and carbon tetrachloride has been obtained from studies of dipole moments. Interaction depends both on the basicity of the amine and on steric factors. Its extent is detected by the difference in total polarisation or dipole moment of the solute in carbon tetrachloride and benzene. Similar interaction occurs with pyridine 1-oxides.

CONSIDERABLE qualitative evidence [1-4] indicates that amines can interact with polyhalogenated methanes. Polarisation studies [5,6] of ethers in tri- and tetra-halogenated methanes have indicated the formation of 1 : 1 complexes in solution, the bonding of the trihalogenated being stronger than that of the tetrahalogenated methanes. Similar results were found for acetone and quinoline.[6] In addition, studies have been made on chloroform–triethylamine mixtures in benzene.[5] It seems that the trihalogenated complexes are held together mainly by hydrogen bonding, whereas in the tetrahalogenated complexes the halogen atoms act as electron acceptors. Pentachloroethane shows as much tendency as chloroform to combine with ether, whereas hexachloroethane behaves in a similar manner to carbon tetrachloride.[6]

In phase equilibrium studies of systems containing pyridine and polyhalogenated methanes VanderWerf and his co-workers [7] detected solid compounds having ratios of base to halogenated methane 3 : 1, 2 : 1, 1 : 1, and 1 : 2. 2,6-Lutidine appears to form only 1 : 1 solid addition compounds. The compounds other than those containing equimolecular proportions seem to be " lattice compounds."

Whilst Raman spectra [8] show that the doublet at 790 cm.$^{-1}$ of carbon tetrachloride shifts in frequency and intensity when liquid ammonia is added, the relaxation time of aniline in carbon tetrachloride solution indicates that any association can be at the most only very weak.[9] The bands corresponding to the symmetric and antisymmetric amino-stretching frequencies of butylamine in carbon tetrachloride and dioxan solution are

[1] Collins, *Chem. and Ind.*, 1957, 704.
[2] Davies, Evans, and Whitehead, *J.*, 1939, 644.
[3] Sharada and Murthy, *Current Sci.*, 1960, **5**, 179.
[4] Cromwell, Foster, and Wheeler, *Chem. and Ind.*, 1959, 228.
[5] Hammick, Norris, and Sutton, *J.*, 1938, 1755.
[6] Earp and Glasstone, *J.*, 1935, 1709, 1720.
[7] Davidson, VanderWerf, and Boatwright, *J. Amer. Chem. Soc.*, 1947, **69**, 3045; VanderWerf, Davidson, and Michaelis, *ibid.*, 1948, **70**, 908.
[8] Kinumaki and Aida, *Sci. Reports Res. Inst. Tohôku Univ.*, 1954, *A*, **6**, 636.
[9] Fischer, *Z. Naturforsch.*, 1954, **9a**, 904.

considerably reduced in intensity in the former solvent, suggesting some form of interaction between the amine and carbon tetrachloride.[10] Partington and Middleton [11] found the dipole moment of pyridine to be abnormally high in carbon tetrachloride and ascribed this to the presence of an interaction between the solvent and solute. Le Fèvre and his co-workers [12] also found an increase in dipole moment of 0·12 D relative to benzene for pyridine and rather smaller differences for quinoline and isoquinoline, but they attributed the difference to an increase in atomic polarisation as a result of solvation rather than to formation of a polar adduct.

Experimental

Apparatus.—Dielectric constants were measured by using a heterodyne capacitance meter based on a circuit described by Weissberger [13] but modified by addition of an oscilloscope to detect the balance point. The apparatus was calibrated with benzene (dielectric constant 2·2725). Capacity changes were followed with a Sullivan Precision Variable Air Condenser, and variations in dielectric constant of 0·0001 could be detected. With the cell in a draught-proof holder, and temperature controlled at 25° ± 0·01°, the maximum drift during at least 0·5 hr. was generally undetectable on the scale of the variable condenser.

Specific volumes were measured in a pyknometer of the type described by Cumper, Vogel, and Walker,[14] the specific volume of benzene being assumed to be 1·14445.

Refractive indices were measured on a Pulfrich refractometer which was supplied with water at 25° from the thermostat-bath.

Preparation and Purification of Materials.—Thiophen-free, crystallisable benzene was shaken with concentrated sulphuric acid, until no browning of the acid layer occurred, washed, shaken with sodium hydroxide solution, and dried (KOH). The benzene was then distilled from sodium in a 70-cm. column packed with glass helices, the middle fraction being collected and refractionated from potassium in a 14-plate column packed with glass helices, a middle fraction again being taken. This fraction was stored in the dark over sodium wire for at least a week before use.

" AnalaR " carbon tetrachloride was refluxed for several hours with 5% sodium hydroxide solution, washed with water, dried ($CaCl_2$; then P_2O_5), and fractionated from phosphoric oxide in a 1-m. column packed with Dixon gauze rings. There was no change in b. p. between the first and the last fraction, but a middle fraction, comprising about two-thirds of the total, was always taken and stored for at least a week in the dark over phosphoric oxide before use.

" Spectroscopic-grade " cyclohexane was passed through silica gel to remove any traces of unsaturated compounds and then fractionated from potassium. A middle fraction was taken, although no change in b. p. occurred. The sample was stored for a week over sodium wire before use.

The following compounds were commercial samples, purified by drying (K_2CO_3) and fractionation from phosphoric oxide in a high-efficiency, low-hold-up column (recorded b. p.s and m. p.s are given in parentheses): piperidine, b. p. 106°/760 mm. (105·6° [15]), butylamine, b. p. 76·5°/765 mm. (76·2° [16]), triethylamine, b. p. 88·5°/755 mm. (89·4° [17]), 2,6-dimethylpyridine (fractionated from boron trifluoride [18]), b. p. 144·5° (144—145° [19]) [picrate, m. p. 163° (163° [19])]. Aniline was a synthetic sample purified as described by Smith [20] and had b. p. 184° (184·4° [17]).

8-Hydroxyquinoline was recrystallised several times from light petroleum (b. p. 60—80°) and had m. p. 75° (75—76° [19]).

[10] Richards and Walker, *Trans. Faraday Soc.*, 1961, **57**, 399.
[11] Partington and Middleton, *Nature*, 1938, 141, 516.
[12] Buckingham, Chau, Freeman, Le Fèvre, Narayana Rao, and Tardif, *J.*, 1956, 1405.
[13] Weissberger, " Physical Methods of Organic Chemistry," Interscience Publ., Inc., New York, 1949, p. 1638.
[14] Cumper, Vogel, and Walker, *J.*, 1956, 3621.
[15] Davies and McGee, *J.*, 1950, 678.
[16] Rogers, *J. Amer. Chem. Soc.*, 1947, **69**, 457.
[17] Timmermans, " Physico-Chemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950.
[18] Brown, Johnson, and Podall, *J. Amer. Chem. Soc.*, 1954, **76**, 5556.
[19] Rodd, " Chemistry of Carbon Compounds," Elsevier, Amsterdam, 1957, Vol. IVa.
[20] Few and Smith, *J.*, 1949, 753.

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The following compounds were prepared by standard methods and purified by fractionation or crystallisation: 4-methylpyridine 1-oxide [21] (from benzene), m. p. 183° (185—186°,[21] 181° [22]) unchanged by further recrystallisation, 4-phenylpyridine [23] (from water), m. p. 77° (77—78° [19]) [picrate, m. p. 196° (195—196° [23])], 4-nitropyridine, m. p. 52° (50° [24]), 3-isopropylpyridine, b. p. 179°/750 mm. (179·3° [25]) [picrate, m. p. 138·5° (138·1—138·6° [25])], 4-t-butylpyridine, b. p. 197°/765 mm. (196·3° [25]) [picrate, m. p. 131° (130·9—131·4° [25])], 2-phenylpyridine,[26] b. p. 270°/760 mm. (268—269° [19]) [picrate, m. p. 175—176° (174—175° [19])], 2,6-diphenylpyridine, m. p. 80—81° (81° [27]) [picrate, m. p. 171° (171° [27])].

4-Methylpyridine, b. p. 144·2°/750 mm. (145·4°/760 mm.[28]) [picrate, m. p. 168—169° (165°, 167°, 168° [19])], and 3-methylpyridine, b. p. 143·5°/755 mm. (144°/755 mm.[28]) [picrate, m. p. 153°

TABLE 1.

Piperidine in benzene

10^6w_2	ε_{12}	v_{12}	n_{12}^2
1264	2·2745	1·14449	2·24352
2560	2·2762	1·14453	2·24343
3992	2·2781	1·14455	2·24305
5425	2·2802	1·14459	2·24292
6402	2·2816	1·14462	2·24274
10,284	2·2874	1·14474	2·24215
10,698	2·2880	1·14474	2·24224

$\varepsilon_{12} = 2{\cdot}2725 + 1{\cdot}4400w_2$;
$v_{12} = 1{\cdot}14445 + 0{\cdot}0273w_2$;
$n_{12}^2 = 2{\cdot}24370 - 0{\cdot}1440w_2$;
${}_2P_\infty = 52{\cdot}78$ c.c.;
$R_D = 26{\cdot}90$ c.c.; $\mu = 1{\cdot}13$ D.

Piperidine in carbon tetrachloride

10^6w_2	ε_{12}	v_{12}	n_{12}^2
1115	2·2318	0·63091	2·12463
1575	2·2338	0·63113	2·12466
2317	2·2362	0·63181	2·12477
2938	2·2385	0·63181	2·12483
3506	2·2404	0·63211	2·12489
4144	2·2432	0·63242	2·12497
6087	2·2501	0·63341	2·12518

$\varepsilon_{12} = 2{\cdot}2276 + 3{\cdot}7266w_2$;
$v_{12} = 0{\cdot}63035 + 0{\cdot}5039w_2$;
$n_{12}^2 = 2{\cdot}12447 + 0{\cdot}1200w_2$;
${}_2P_\infty = 61{\cdot}62$ c.c.
$R_D = 27{\cdot}46$ c.c.; $\mu = 1{\cdot}29$ D.

Butylamine in carbon tetrachloride

10^6w_2	ε_{12}	v_{12}	n_{12}^2
569	2·2304	0·63081	2·12332
1809	2·2371	0·63170	2·12302
2011	2·2387	0·63185	2·12291
2871	2·2431	0·63253	2·12279
3362	2·2458	0·63284	2·12262
4951	2·2545	0·63398	2·12232
6313	2·2620	0·63497	2·12200

$\varepsilon_{12} = 2{\cdot}2272 + 5{\cdot}5377w_2$;
$v_{12} = 0{\cdot}63040 + 0{\cdot}7256w_2$;
$n_{12}^2 = 2{\cdot}12343 - 0{\cdot}2298w_2$;
${}_2P_\infty = 71{\cdot}65$ c.c.;
$R_D = 25{\cdot}15$ c.c.; $\mu = 1{\cdot}51$ D.

Triethylamine in carbon tetrachloride *

10^6w_2	ε_{12}	v_{12}	n_{12}^2
833	2·2280	0·63091	—
1824	2·2290	0·63169	—
2950	2·2304	0·63243	—
4592	2·2327	0·63368	—
6491	2·2351	0·63503	—
7959	2·2368	0·63610	—

$\varepsilon_{12} = 2{\cdot}2268 + 1{\cdot}2617w_2$;
$v_{12} = 0{\cdot}63035 + 0{\cdot}0177w_2$;
${}_2P_\infty = 53{\cdot}16$ c.c.;
$R_D = 33{\cdot}74$ c.c.; $\mu = 0{\cdot}98$ D.

* Because crystals of triethylamine hydrochloride appear within an hour of mixing, the dielectric constant and specific volume of each solution were measured immediately after mixing and the molar refractivity was calculated from bond data. The dielectric constant of a mixture of triethylamine and carbon tetrachloride did not alter by a significant factor during the total time taken for each set of measurements.

4-Methylpyridine in carbon tetrachloride

10^6w_2	ε_{12}	v_{12}	n_{12}^2
759	2·2391	0·63069	2·12365
1311	2·2476	0·63094	2·12384
2006	2·2584	0·63119	2·12401
3015	2·2747	0·63159	2·12428
3414	2·2815	0·63179	2·12448
4271	2·2945	0·63209	2·12474
6582	2·3307	0·63305	2·12538

$\varepsilon_{12} = 2{\cdot}2270 + 15{\cdot}8017w_2$;
$v_{12} = 0{\cdot}63038 + 0{\cdot}4064w_2$;
$n_{12}^2 = 2{\cdot}12342 + 0{\cdot}3015w_2$;
${}_2P_\infty = 183{\cdot}77$ c.c.;
$R_D = 29{\cdot}43$ c.c.; $\mu = 2{\cdot}75$ D.

4-Methylpyridine in cyclohexane

10^6w_2	ε_{12}	v_{12}	n_{12}^2
1416	2·0220	1·29375	2·02479
3274	2·0330	1·29338	2·02490
4700	2·0419	1·29310	2·02510
5661	2·0487	1·29296	2·02541
6771	2·0557	1·29275	2·02558
7970	2·0627	1·29249	2·02575
10,866	2·0805	1·29192	2·02610

$\varepsilon_{12} = 2{\cdot}0128 + 6{\cdot}2695w_2$;
$v_{12} = 1{\cdot}29402 - 0{\cdot}1916w_2$;
$n_{12}^2 = 2{\cdot}02445 + 0{\cdot}1594w_2$;
${}_2P_\infty = 166{\cdot}66$ c.c.;
$R_D = 29{\cdot}69$ c.c.; $\mu = 2{\cdot}59$ D.

4-t-Butylpyridine in carbon tetrachloride

10^6w_2	ε_{12}	v_{12}	n_{12}^2
923	2·2365	0·63076	2·12372
1726	2·2473	0·63115	2·12387
2675	2·2588	0·63158	2·12434
4127	2·2755	0·63220	2·12469
5916	2·2971	0·63303	2·12524
8828	2·3311	0·63432	2·12571
10,610	2·3530	0·63513	2·12626

$\varepsilon_{12} = 2{\cdot}2266 + 11{\cdot}8692w_2$;
$v_{12} = 0{\cdot}63035 + 0{\cdot}4517w_2$;
$n_{12}^2 = 2{\cdot}12343 + 0{\cdot}2822w_2$;
${}_2P_\infty = 212{\cdot}33$ c.c.;
$R_D = 44{\cdot}10$ c.c.; $\mu = 2{\cdot}87$ D.

3-Methylpyridine in carbon tetrachloride

10^6w_2	ε_{12}	v_{12}	n_{12}^2
1039	2·2413	0·63079	2·12353
1679	2·2497	0·63107	2·12404
2896	2·2662	0·63154	2·12436
3850	2·2793	0·63193	2·12471
5344	2·2998	0·63253	2·12530
5400	2·3007	0·63256	2·12533
7677	2·3306	0·63348	2·12606

$\varepsilon_{12} = 2{\cdot}2270 + 13{\cdot}5769w_2$;
$v_{12} = 0{\cdot}63038 + 0{\cdot}4031w_2$;
$n_{12}^2 = 2{\cdot}12342 + 0{\cdot}3367w_2$;
${}_2P_\infty = 161{\cdot}75$ c.c.;
$R_D = 29{\cdot}71$ c.c.; $\mu = 2{\cdot}54$ D.

[21] Boeckelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1286.
[22] Ochiai, *J. Pharm. Soc. Japan*, 1944, **64**, 72.
[23] Haworth, Heilbron, and Hey, *J.*, 1940, 349.
[24] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[25] Brown and Murphey, *J. Amer. Chem. Soc.*, 1951, **73**, 3308.
[26] Gilman and Blatt, *Org. Synth.*, Coll. Vol. II.
[27] Heilbron, "Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1936.
[28] Biddiscombe, Coulson, Handley, and Herington, *J.*, 1954, 1957.

TABLE 1. (*Continued.*)

10^6w_2	ε_{12}	v_{12}	n_{12}^2
3-Methylpyridine in benzene			
2181	2·2872	1·14426	2·24276
3424	2·2956	1·14413	2·24274
5834	2·3116	1·14387	2·24274
6438	2·3163	1·14385	2·24280
7108	2·3213	1·14377	2·24276
11,181	2·3478	1·14335	2·24281
12,455	2·3571	1·14320	2·24284

$\varepsilon_{12} = 2{\cdot}2725 + 6{\cdot}7749w_2$;
$v_{12} = 1{\cdot}14447 - 0{\cdot}1000w_2$;
$n_{12}^2 = 2{\cdot}24271 + 0{\cdot}0082w_2$;
${}_2P_\infty = 147{\cdot}63$ c.c.;
$R_D = 28{\cdot}50$ c.c.; $\mu = 2{\cdot}41$ D.

3-Isopropylpyridine in carbon tetrachloride			
614	2·2334	0·63063	2·12305
1143	2·2388	0·63086	2·12337
2683	2·2540	0·63151	2·12372
3573	2·2641	0·63192	2·12396
4263	2·2714	0·63224	2·12431
5075	2·2801	0·63263	2·12448
5885	2·2884	0·63298	2·12483

$\varepsilon_{12} = 2{\cdot}2266 + 10{\cdot}5012w_2$;
$v_{12} = 0{\cdot}63035 + 0{\cdot}4442w_2$;
$n_{12}^2 = 2{\cdot}12296 + 0{\cdot}3013w_2$;
${}_2P_\infty = 172{\cdot}49$ c.c.;
$R_D = 39{\cdot}53$ c.c.; $\mu = 2{\cdot}55$ D.

3-Isopropylpyridine in benzene			
1429	2·2796	1·14437	2·24247
2963	2·2880	1·14428	2·24242
4509	2·2957	1·14417	2·24233
6002	2·3034	1·14408	2·24230
7218	2·3101	1·14399	2·24224
8723	2·3183	1·14390	2·24221
12,408	2·3372	1·14366	2·24207

$\varepsilon_{12} = 2{\cdot}2723 + 5{\cdot}2300w_2$;
$v_{12} = 1{\cdot}14446 - 0{\cdot}0638w_2$;
$n_{12}^2 = 2{\cdot}24253 - 0{\cdot}0386w_2$;
${}_2P_\infty = 158{\cdot}20$ c.c.;
$R_D = 37{\cdot}45$ c.c.; $\mu = 2{\cdot}43$ D.

2,6-Dimethylpyridine in carbon tetrachloride			
1081	2·2332	0·63086	2·12358
2330	2·2402	0·63141	2·12375
3599	2·2477	0·63199	2·12401
6033	2·2617	0·63305	2·12454
7673	2·2712	0·63378	2·12504
11,176	2·2911	0·63539	2·12576
15,129	2·3139	0·63716	2·12661

$\varepsilon_{12} = 2{\cdot}2270 + 5{\cdot}7421w_2$;
$v_{12} = 0{\cdot}63035 + 0{\cdot}4507w_2$;
$n_{12}^2 = 2{\cdot}12326 + 0{\cdot}2227w_2$;
${}_2P_\infty = 98{\cdot}74$ c.c.;
$R_D = 34{\cdot}21$ c.c.; $\mu = 1{\cdot}78$ D.

2,6-Dimethylpyridine in benzene			
1549	2·2769	1·14438	2·24326
3707	2·2825	1·14426	2·24331
5662	2·2879	1·14416	2·24352
7752	2·2938	1·14405	2·24364
9144	2·2977	1·14397	2·24375
11,085	2·3028	1·14386	2·24382
13,450	2·3096	1·14373	2·24391

$\varepsilon_{12} = 2{\cdot}2725 + 2{\cdot}7450w_2$;
$v_{12} = 1{\cdot}14446 - 0{\cdot}0537w_2$;
$n_{12}^2 = 2{\cdot}24318 + 0{\cdot}0564w_2$;
${}_2P_\infty = 90{\cdot}13$ c.c.;
$R_D = 35{\cdot}39$ c.c.; $\mu = 1{\cdot}64$ D.

4-Phenylpyridine in carbon tetrachloride			
1007	2·2368	0·63061	2·12407
2383	2·2498	0·63095	2·12518
2446	2·2500	0·63097	2·12515
4220	2·2665	0·63143	2·12661
5346	2·2773	0·63172	2·12754
6312	2·2862	0·63197	2·12810
9255	2·3133	0·63272	2·13017

$\varepsilon_{12} = 2{\cdot}2273 + 9{\cdot}3255w_2$;
$v_{12} = 0{\cdot}63035 + 0{\cdot}2557w_2$;
$n_{12}^2 = 2{\cdot}12342 + 0{\cdot}7388w_2$;
${}_2P_\infty = 193{\cdot}07$ c.c.;
$R_D = 50{\cdot}22$ c.c.; $\mu = 2{\cdot}64$ D.

4-Phenylpyridine in benzene			
1008	2·2772	1·14427	2·24227
1617	2·2806	1·14412	2·24240
3216	2·2881	1·14369	2·24278
4682	2·2948	1·14339	2·24326
5353	2·2984	1·14317	2·24349
7781	2·3097	1·14260	2·24427
8688	2·3147	1·14238	2·24433

$\varepsilon_{12} = 2{\cdot}2725 + 4{\cdot}8230w_2$;
$v_{12} = 1{\cdot}14446 - 0{\cdot}2350w_2$;
$n_{12}^2 = 2{\cdot}24192 + 0{\cdot}2745w_2$;
${}_2P_\infty = 182{\cdot}81$ c.c.;
$R_D = 50{\cdot}16$ c.c.; $\mu = 2{\cdot}55$ D.

2-Phenylpyridine in carbon tetrachloride			
1332	2·2330	0·63076	2·12355
2596	2·2399	0·63111	2·12436
3894	2·2464	0·63150	2·12547
5656	2·2557	0·63195	2·12687
6444	2·2605	0·63219	2·12743
8781	2·2718	0·63279	2·12961
10,385	2·2808	0·63331	2·13093

$\varepsilon_{12} = 2{\cdot}2260 + 5{\cdot}2728w_2$;
$v_{12} = 0{\cdot}63040 + 0{\cdot}2766w_2$;
$n_{12}^2 = 2{\cdot}12250 + 0{\cdot}7859w_2$;
${}_2P_\infty = 127{\cdot}48$ c.c.;
$R_D = 51{\cdot}88$ c.c.; $\mu = 1{\cdot}92$ D.

2-Phenylpyridine in benzene			
2281	2·2788	1·14392	2·24355
4655	2·2855	1·14334	2·24430
6878	2·2920	1·14284	2·24513
9375	2·2988	1·14221	2·24613
10,042	2·3007	1·14207	2·24619
11,959	2·3060	1·14158	2·24679
15,443	2·3160	1·14077	2·24813

$\varepsilon_{12} = 2{\cdot}2725 + 2{\cdot}8087w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}2378w_2$;
$n_{12}^2 = 2{\cdot}24277 + 0{\cdot}3478w_2$;
${}_2P_\infty = 123{\cdot}88$ c.c.;
$R_D = 51{\cdot}52$ c.c.; $\mu = 1{\cdot}88$ D.

2,6-Diphenylpyridine in carbon tetrachloride			
578	2·2289	0·63060	2·12469
1102	2·2301	0·63068	2·12489
1560	2·2310	0·63079	2·12521
2554	2·2335	0·63102	2·12591
4053	2·2375	0·63137	2·12704
4606	2·2388	0·63151	2·12740
5290	2·2406	0·63167	2·12798

$\varepsilon_{12} = 2{\cdot}2271 + 2{\cdot}5679w_2$;
$v_{12} = 0{\cdot}63042 + 0{\cdot}2381w_2$;
$n_{12}^2 = 2{\cdot}12410 + 0{\cdot}7304w_2$;
${}_2P_\infty = 121{\cdot}17$ c.c.;
$R_D = 73{\cdot}53$ c.c.; $\mu = 1{\cdot}53$ D.

2,6-Diphenylpyridine in benzene			
1941	2·2755	1·14391	2·24445
3052	2·2770	1·14359	2·24475
4768	2·2797	1·14315	2·24541
5893	2·2814	1·14279	2·24592
7744	2·2842	1·14228	2·24676
8486	2·2853	1·14207	2·24703
9473	2·2867	1·14180	2·24730

$\varepsilon_{12} = 2{\cdot}2725 + 1{\cdot}5064w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}2795w_2$;
$n_{12}^2 = 2{\cdot}24364 + 0{\cdot}3903w_2$;
${}_2P_\infty = 125{\cdot}11$ c.c.;
$R_D = 75{\cdot}83$ c.c.; $\mu = 1{\cdot}55$ D.

4-Nitropyridine in carbon tetrachloride			
805	2·2305	0·63049	2·12334
2079	2·2356	0·63065	2·12390
2826	2·2388	0·63074	2·12413
3918	2·2433	0·63090	2·12469
4815	2·2467	0·63101	2·12489
5406	2·2491	0·63110	2·12533
7292	2·2567	0·63133	2·12582

$\varepsilon_{12} = 2{\cdot}2273 + 4{\cdot}0379w_2$;
$v_{12} = 0{\cdot}63038 + 0{\cdot}1312w_2$;
$n_{12}^2 = 2{\cdot}12302 + 0{\cdot}4038w_2$;
${}_2P_\infty = 80{\cdot}47$ c.c.;
$R_D = 31{\cdot}32$ c.c.; $\mu = 1{\cdot}55$ D.

8-Hydroxyquinoline in carbon tetrachloride			
665	2·2325	0·63053	2·12422
1039	2·2366	0·63061	2·12445
1784	2·2438	0·63077	2·12495
1954	2·2450	0·63080	2·12504
2616	2·2521	0·63093	2·12538
2739	2·2532	0·63096	2·12556
3548	2·2615	0·63112	2·12614

$\varepsilon_{12} = 2{\cdot}2260 + 9{\cdot}9614w_2$;
$v_{12} = 0{\cdot}63040 + 0{\cdot}2036w_2$;
$n_{12}^2 = 2{\cdot}12378 + 0{\cdot}6469w_2$;
${}_2P_\infty = 188{\cdot}24$ c.c.;
$R_D = 43{\cdot}43$ c.c.; $\mu = 2{\cdot}66$ D.

Aniline in carbon tetrachloride			
1629	2·2352	0·63099	2·12530
3409	2·2438	0·63167	2·12620
5271	2·2534	0·63236	2·12743
6982	2·2620	0·63302	2·12839
8197	2·2679	0·63347	2·12924
10,072	2·2782	0·63420	2·13029
10,966	2·2826	0·63452	2·13093

$\varepsilon_{12} = 2{\cdot}2265 + 5{\cdot}1068w_2$;
$v_{12} = 0{\cdot}63038 + 0{\cdot}3776w_2$;
$n_{12}^2 = 2{\cdot}12427 + 0{\cdot}5995w_2$;
${}_2P_\infty = 77{\cdot}59$ c.c.;
$R_D = 31{\cdot}79$ c.c.; $\mu = 1{\cdot}50$ D.

Pyridine 1-oxide in benzene			
1209	2·2964	1·14398	2·24385
2069	2·3129	1·14368	2·24415
3639	2·3452	1·14313	2·24478
3648	2·3467	1·14312	2·24454
6607	2·4048	1·14203	2·24553
7442	2·4245	1·14172	2·24577
9841	2·4726	1·14084	2·24661

$\varepsilon_{12} = 2{\cdot}2720 + 20{\cdot}2318w_2$;
$v_{12} = 1{\cdot}14444 - 0{\cdot}3651w_2$;
$n_{12}^2 = 2{\cdot}24350 + 0{\cdot}3114w_2$;
${}_2P_\infty = 383{\cdot}95$ c.c.;
$R_D = 27{\cdot}36$ c.c.; $\mu = 4{\cdot}18$ D.

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TABLE 1. (*Continued.*)

10^4w_2	ε_{12}	v_{12}	n_{12}^2
Pyridine 1-oxide in cyclohexane †			
0	2·0130	1·29374	—
70	2·0141	1·29371	—
258	2·0171	1·29366	—
328	2·0183	1·29363	—
556	2·0217	1·29355	—

$\varepsilon_{12} = 2{\cdot}0130 + 15{\cdot}84w_2$;
$v_{12} = 1{\cdot}29374 - 0{\cdot}338w_2$;
$_2P_\infty = 386{\cdot}0$ c.c.;
$\mu = 4{\cdot}19 \pm 0{\cdot}03$ D.

† Several other solutions which were prepared gave precipitates before measurement was complete. The R_D value obtained for benzene solution was used in calculating μ.

10^4w_2	ε_{12}	v_{12}	n_{12}^2
4-Methylpyridine 1-oxide in carbon tetrachloride ‡			
16	2·2344	0·63039	
50	2·2494	0·63045	—
50	2·2497	0·63046	—
95	2·2695	0·63054	—
108	2·2759	0·63057	—
120	2·2804	0·63059	—
131	2·2851	0·63062	—

$\varepsilon_{12} = 2{\cdot}2272 + 44{\cdot}56w_2$;
$v_{12} = 0{\cdot}63036 + 0{\cdot}193w_2$;
$_2P_\infty = 540{\cdot}7$ c.c.;
$\mu = 4{\cdot}97 \pm 0{\cdot}03$ D.

‡ The R_D value for benzene solution was used. The lines obtained show that quoting weight fractions to the accuracy expressed here is acceptable.

10^4w_2	ε_{12}	v_{12}	n_{12}^2
4-Methylpyridine 1-oxide in benzene			
785	2·2882	1·14417	2·24421
1479	2·3033	1·14394	2·24445
1823	2·3101	1·14381	2·24451
2727	2·3292	1·14357	2·24495
2875	2·3317	1·14352	2·24505
3242	2·3388	1·14340	2·24517
4491	2·3644	1·14303	2·24565

$\varepsilon_{12} = 2{\cdot}2725 + 20{\cdot}5600w_2$;
$v_{12} = 1{\cdot}14442 - 0{\cdot}3163w_2$;
$n_{12}^2 = 2{\cdot}24384 + 0{\cdot}4052w_2$;
$_2P_\infty = 448{\cdot}90$ c.c.;
$R_D = 34{\cdot}92$ c.c.; $\mu = 4{\cdot}50$ D.

TABLE 2. *Dipole moments at 25°.*

	μ_B (D)	μ_{CT} (D)	μ_{CH} (D)	Lit.
Butylamine	—	1·51		
Piperidine	—	1·29		
Triethylamine	—	0·98		
4-Methylpyridine	—	2·75	2·59	B 2·60 [a]
4-t-Butylpyridine	—	2·87		B 2·73 [a]
2,6-Dimethylpyridine	1·64	1·78		B 1·65,[b] 1·66 [a]
3-Methylpyridine	2·41	2·54		B 2·40 [a]
3-Isopropylpyridine	2·43	2·55		
4-Phenylpyridine	2·55	2·64		
2-Phenylpyridine	1·88	1·92		
4-Nitropyridine	—	1·55		
2,6-Diphenylpyridine	1·55	1·53		
8-Hydroxyquinoline	—	1·86		
Aniline	—	1·50		CT 1·48 [c]
4-Methylpyridine 1-oxide	4·50	4·97		B 4·74 [d]
Pyridine 1-oxide	4·18	—	4·19	B 4·24 [e]

[a] See ref. 14. [b] Goethals (*Rec. Trav. chim.*, 1935, **54**, 299. [c] Few and Smith's figures (*J.*, 1949, 3057) recalculated, with $P_E + P_A = R_D$. [d] Katritzky, Randall, and Sutton, *J.*, 1957, 1769. [e] Linton, *J. Amer. Chem. Soc.*, 1940, **62**, 1945.

(153° [29])], were prepared by reduction of the appropriate methylpyridine 1-oxide with phosphorus trichloride followed by drying and fractionation in the column mentioned.[30]

In all cases, solid samples were stored under a high vacuum in the dark and in the presence of phosphoric oxide and wax shavings for at least 2 days before use. For deliquescent compounds, the desiccator was refilled with dry nitrogen before opening. Liquids were used immediately after distillation, or, where this was not possible, stored in small Quickfit stoppered flasks with a minimum of air-space and in the dark.

Results.—At least six solutions varying in weight fraction between 0·001 and 0·015 were used in each determination of dipole moment. Solute–solute interactions have been assumed to be negligible in this concentration range, and in all cases the plots of dielectric constant (ε_{12}), specific volume (v_{12}), and squares of the refractive indices (n_{12}^2) against their weight fractions showed no deviation from linearity. The equations employed were $\varepsilon_{12} = \varepsilon_1 + \alpha w_2$, $v_{12} = v_1 + \beta w_2$, and $n_{12}^2 = n_1^2 + \gamma w_2$, where α, β, and γ were calculated from the quotients shown below in order to avoid giving undue weight to the results in the most dilute solutions:

$$\alpha = \sum(\varepsilon_{12} - \varepsilon_1)/\sum w_2, \qquad \beta = \sum(v_{12} - v_1)/\sum w_2, \qquad \gamma = \sum(n_{12}^2 - n_1^2)/\sum w_2$$

[29] Coulson and Jones, *J. Soc. Chem. Ind.*, 1946, **65**, 169.
[30] Ray, *Rev. Sci. Instr.*, 1957, **28**, 200.

TABLE 3. *Polarisation, relative polarisation, and dipole-moment changes.*

	$_2P_\infty$ (B) (c.c.)	$_2P_\infty$(CT) (c.c.)	ΔP (c.c.)	$\Delta P/{}_2P_\infty$ (B)	μ_B (D)	μ_{CT} (D)	$\Delta\mu$ (D)	pK_a
Butylamine	61·13 [b]	71·65 [a]	+10·52	0·172	1·34	1·51	+0·17	10·6 [i]
Piperidine	52·78 [a]	61·62 [a]	+8·84	0·167	1·13	1·29	+0·16	11·1 [j]
Triethylamine	50·10 [c]	53·16 [a]	+3·06	0·061	0·91	0·98	+0·07	10·78 [k]
4-Methylpyridine	167·88 [d]	183·77 [a]	+15·89	0·095	2·60	2·75	+0·15	6·02 [l]
4-t-Butylpyridine	195·26 [d]	212·33 [a]	+17·07	0·087	2·73	2·87	+0·14	5·99 [l]
2,6-Dimethylpyridine	90·13 [a]	98·74 [a]	+8·61	0·096	1·64	1·78	+0·14	6·75 [l]
3-Methylpyridine	147·63 [a]	161·75 [a]	+14·12	0·096	2·41	2·54	+0·13	5·68 [l]
3-Isopropylpyridine	158·20 [a]	172·49 [a]	+14·29	0·090	2·43	2·55	+0·12	5·72 [l]
Pyridine	127·8 [e]	138·8 [e]	+11·0	0·086	2·25	2·37	+0·12	5·29 [m]
4-Phenylpyridine	182·81 [a]	193·07 [a]	+10·26	0·056	2·55	2·64	+0·09	—
2-Phenylpyridine	123·88 [a]	127·48 [a]	+3·60	0·029	1·88	1·92	+0·04	—
4-Nitropyridine	82·00 [f]	80·47 [a]	−1·53	−0·019	1·58	1·55	−0·03	—
Isoquinoline	181·0 [g]	184·4 [g]	+3·4	0·019	2·61	2·65	+0·04	5·14 [j]
Quinoline	144·4 [g]	147·1 [g]	+2·7	0·019	2·24	2·27	+0·03	4·94 [j]
2,6-Diphenylpyridine	125·11 [a]	121·17 [a]	−3·94	−0·031	1·55	1·53	−0·02	—
8-Hydroxyquinoline	191·48 [g]	188·24 [a]	−3·24	−0·017	2·68	2·66	−0·02	—
Aniline	78·35 [h]	77·59 [a]	−0·76	−0·010	1·53	1·50	−0·03	4·58 [i]
4-Methylpyridine 1-oxide	448·90 [a]	540·71 [a]	+91·81	0·205	4·50	4·97	+0·47	—

B = Benzene. CT = Carbon tetrachloride.

$\Delta P = {}_2P_\infty$ (in CT) − $_2P_\infty$ (in B). $\Delta\mu = \mu$ (in CT) − μ (in B).

[a] This investigation. [b] Few and Smith's figures (*J.*, 1949, 2663) recalculated with $R_D = P_E + P_A$. Barclay, Le Fèvre, and Smythe (*Trans. Faraday Soc.*, 1950, **46**, 812). [c] Cumper, Vogel, and Walker.[14] [d] Buckingham, Le Fèvre, *et al.*[13] [e] Katritzky, Randall, and Sutton (*J.*, 1957, 1769). [f] Richards and Walker.[10] [g] Few and Smith, *J.*, 1949, 3057. [h] Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469. [i] From Rodd.[20] [j] Dilke, Eley, and Sheppard, *Trans. Faraday Soc.*, 1950, **46**, 261. [k] Brown and Mihm, *J. Amer. Chem. Soc.*, 1955, **77**, 1723. [l] Jaffé and Doak, *ibid.*, p. 4441.

The molar polarisation ($_2P_\infty$) and R_D value at infinite dilution were calculated from the equations:

$$_2P_\infty = M_2[3\alpha v_1/(\varepsilon_1 + 2)^2 + (\varepsilon_1 - 1)(v_1 + \beta)/(\varepsilon_1 + 2)]$$

$$R_D = M_2[3\gamma v_1/(n_1^2 + 2)^2 + (n_1^2 - 1)(v_1 + \beta)/(n_1^2 + 2)]$$

where ε_1 was taken as 2·2725, n_1^2 as 2·24331, and v_1 as 1·14445. The dipole moment (μ) was obtained from the usual relation, $\mu = 0{\cdot}01281(P_0T)^{\frac{1}{2}}$. P_0 was calculated by assuming that $P_E + P_A = R_D$. In fact, R_D is less than $P_E + P_A$, and the true dipole moment values are inexact to this extent. If, however, the P_A values are not strongly solvent-dependent, then the resultant dipole-moment difference is not greatly in error.

Tables 1—3 give detailed results.

DISCUSSION

Table 3 shows that the difference in moment between carbon tetrachloride and benzene solution ($\Delta\mu$) varies from slightly negative to 0·17 D for the amines, and to 0·47 D for 4-methylpyridine 1-oxide. The differences in total polarisation range up to 17·1 c.c. for the amines. Changes in total polarisation of this magnitude are unlikely to be solely due to increases in atomic polarisation, as suggested by Le Fèvre and his co-workers. The change in total polarisation of 4-methylpyridine 1-oxide (91·8 c.c.) is nearly three times the R_D value of that compound in benzene. Further, the known P_A and P_E values for pyridine are 1·5 and 23·0 c.c. respectively.[31] An increment of 11·0 c.c. in P_A for this compound in carbon tetrachloride is hardly conceivable. The dipole moments can best be explained by a donor–acceptor type of interaction, a transient increase in polarisation occurring as carbon tetrachloride molecules approach the vicinity of the lone-pair electrons of the nitrogen atom. Such an interaction would increase the total polarisation of the system, partly by increasing the atomic polarisation of the interacting molecules and partly by a change in dipole moment. The alternative explanation of the dipole moment differences as being due to interaction of the amines with the π-electron clouds of benzene can be discounted because of the similarity of the dipole moments of 4-methylpyridine,

[31] Cartwright and Errera, *J. Proc. Roy. Soc.*, 1936, *A*, **154**, 138.

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and also of pyridine 1-oxide, in benzene and cyclohexane. There are other cases to support this.[32]

The observed increase should depend on two factors: (i) The stability of the adduct, where the total polarisation might be expected to increase as the basicity of the amine increases. The $\Delta\mu$ values would then show some dependence on the pK_a of the amine. If $\Delta\mu$ or ΔP is plotted against pK_a an approximately straight line is obtained for those molecules where the steric factors in the 2- and the 6-position are small. (ii) Since the bonding cannot be very strong, the number of solvent molecules passing near the nitrogen atom should depend on the total volume of approach that is available. The effect should, thus, be very dependent on steric factors. The steric effect is lowest in pyridines having no 2-substituent; this may account for their $\Delta\mu$ values which are high in relation to basicity.

The steric effect is well illustrated by 2-substituted pyridines. A 2-phenyl group cuts off about half the approach that is available in pyridine itself, although the basicity can hardly alter greatly. The $\Delta\mu$ value (0·04 D) is considerably less than that of pyridine. A second phenyl group (in the 6-position) almost completely blocks the approach of carbon tetrachloride molecules: the $\Delta\mu$ value is then −0·02 D. A slightly negative value was also found for aniline and 8-hydroxyquinoline, in both of which interaction can be expected to be negligible. Although 2,6-dimethylpyridine has a higher pK_a than pyridine, the steric effect of the two methyl groups limits the increase in dipole moment which might be expected (0·14 D). The steric effect of the methyl groups in this compound has been previously reported.[33]

The $\Delta\mu$ value for 4-nitropyridine is −0·03 D, but since the total dipole moment acts in the opposite direction to the nitrogen lone-pair dipole, the value required for comparison is +0·03 D. A low value would be expected in view of the probable reduction in basic strength as a result of electron-withdrawal by the nitro-group. Similar $\Delta\mu$ values are found for quinoline and isoquinoline which have lower basicities than pyridine.

In aliphatic amines, the alkyl groups and the amino-hydrogen atoms considerably obstruct the approach of carbon tetrachloride molecules, reducing the effect of their high basicity. In butylamine ($\Delta\mu$ 0·17 D) there are a number of rotational configurations in which approach is blocked.

It is impossible for the three ethyl groups all to lie " behind " the nitrogen atom at the same time in triethylamine; one of the groups must project over the nitrogen atom, thus shielding it from the approach of carbon tetrachloride molecules. As was expected, the $\Delta\mu$ value (0·07 D) was less than that of butylamine. The effect of the three ethyl groups in hindering the formation of co-ordination compounds has been previously reported.[34]

Piperidine has the highest basicity of the amines considered here, but again approach to the nitrogen atom is considerably restricted, not only by the adjacent CH_2 groups and the amino-hydrogen atom, but also by the remainder of the molecule since the ring is puckered. The $\Delta\mu$ value (0·16 D) appears reasonable in view of this.

Physical evidence indicates that the interaction of aniline with carbon tetrachloride is negligible.[9] The basicity is low, and approach to the nitrogen atom is also hampered by the amino-hydrogen atoms. The $\Delta\mu$ value found was −0·03 D. Infrared [35] and dipole-moment work [10] indicates that 8-hydroxyquinoline is strongly intramolecularly hydrogen bonded. Formation of any complex involving the lone pair of the nitrogen atom is, thus, not feasible. The $\Delta\mu$ value was −0·02 D, in accord with the values obtained for aniline and 2,6-diphenylpyridine. In these cases, this small negative value appears to be the straightforward solvent effect.

[32] See Wesson, " Tables of Electric Dipole Moments," Technology Press, Massachusetts, 1948.
[33] Braude and Nachod, " Determination of Organic Structures by Physical Methods," Academic Press, New York, 1955, p. 640.
[34] Ref. 33, p. 642.
[35] Bellamy and Hallam, *Trans. Faraday Soc.*, 1959, **55**, 220.

The dipole-moment values obtained for pyridine 1-oxide and 4-methylpyridine 1-oxide differ from reported values because of complete exclusion of water. The effect of traces of moisture on the dipole moments of the pyridine oxides will be discussed in a later paper. The result indicates that a large increase in dipole moment may occur in carbon tetrachloride solution. This is not unreasonable, since the compounds are basic and the oxygen atoms may act as donors in a number of co-ordination complexes.[36] Moreover, there are two sets of lone-pair electrons on the oxygen atom, which extend well away from the bulk of the molecule and so are more favourably placed for interaction with carbon tetrachloride molecules.

The results as a whole are consistent with the concept of donor–acceptor interaction where carbon tetrachloride is the acceptor. Such interaction should be exothermic, and the heats of mixing of a number of substituted pyridines with benzene and carbon tetrachloride are at present being measured. The results so far agree well with the conclusions from dipole moments, the heat of mixing with benzene being small and mainly negative, but with carbon tetrachloride appreciably positive; the quantity of heat evolved is higher for compounds with high $\Delta\mu$ values.

One of us (A. N. S.) is indebted to the Department of Scientific and Industrial Research for a maintenance grant. We express our gratitude to Mr. L. P. Priestly, the Head of this Department, for his interest and support, also to Mr. A. Clarke for technical assistance.

School of Chemistry, College of Technology,
Leicester. [*Received, November 1st*, 1960.]

[36] Katritzky and Lagowski, "Heterocyclic Chemistry," Methuen, London, 1960, p. 104.

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572. *The* $PtCl_6^{2-}$–I^- *and* $PtBr_6^{2-}$–I^- *Replacement Reactions.*

By A. J. Poë and M. S. Vaidya.

The replacement reactions of iodide ions with $PtCl_6^{2-}$ and $PtBr_6^{2-}$ ions have been studied by radio-tracer and spectrophotometric methods. In the presence of $IrCl_6^{2-}$, the reactions are of first order in both iodide and Pt–Cl or Pt–Br bond concentrations, and probably involve an S_N2 mechanism. For the $PtCl_6^{2-}$–I^- reaction, $k_{25} = 0{\cdot}85 \pm 0{\cdot}05$ l. mole^{-1} min.$^{-1}$, the rate-determining step being the replacement of the first chloride ligand. The $PtBr_6^{2-}$–I^- reaction, at 1°, has a rate constant of about 12 l. mole^{-1} min.$^{-1}$ for replacement of the first two bromide ligands, but subsequent reaction is slower. Increasing lability along the series chloro-, bromo-, and iodo-platinate is ascribed, in part at least, to decreasing bond strengths.

In the absence of $IrCl_6^{2-}$, the reactions are faster and are photosensitive. The $PtCl_6^{2-}$–I^- reaction is greatly accelerated by small amounts of thiosulphate and of ferrous ions, and Pt(III) intermediates are probably formed. Chloroplatinate, containing a negligible quantity of iridium, exchanges relatively slowly with chloride ions and the reaction is greatly accelerated by very small amounts of thiosulphate.

Replacement reactions of a series of related complex ions with a single ligand species can give more information about the differing natures of the complexes than can the ligand exchange reactions in which both reactants change from case to case.[1] We have therefore studied the reactions of hexachloro-, hexabromo-, and hexaiodo-platinates with iodide ion. In addition, it was hoped that the relative reactivity of the intermediate mixed halogeno-complexes would throw some light on the relative effects of the halide ligands on the reactivity of other Pt(IV)–Hal bonds in the same ion. The PtI_6^{2-}–I^-

[1] Zvyagintsev and Karandasheva, *Proc. Acad. Sci. (U.S.S.R.)*, 1956, **108**, 277.

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exchange reaction has already been described [2] and results for the two replacement reactions have been reported briefly.[3]

The replacement reactions are reversible but the equilibrium constants are such that the reverse reactions have negligible kinetic effect.[4] The reactions were studied by making use of the insolubility of cæsium hexahalogenoplatinates and by using radioactive $^{131}I^-$ to indicate the extent of uptake of iodide by the complex. The replacement reactions involve a changing proportion of various mixed halogeno-complexes, and each of these would be expected to exhibit a characteristic rate constant in its reaction with iodide ions. To simplify this kinetic problem the reactions were considered to be between the iodide ions and Pt–Cl or Pt–Br bonds and the effects of the other ligands attached to the platinum were ignored. In this way statistical effects were eliminated and any transmitted effects due to the other ligands would be expected to be revealed by changes in the derived "rate constants" during the reactions. The order of the reaction could be determined by comparing the rate constants, calculated according to the first- or second-order rate-equations from data obtained at different initial concentrations.

Results

The $PtCl_6^{2-}$–I^- *Reaction.*—Recent confirmatory runs,[5] performed some time after the main group [3] of experiments had been completed and making use of a recently obtained chloroplatinate sample, showed that the reaction is both light-sensitive and inhibited by the addition of small amounts of hexachloroiridate ions. The reaction observed in the presence of 1—5% of hexachloroiridate conformed to the earlier results, some of which are given in Table 1. These show no effects caused by laboratory light or hexachloroiridate, and an inhibitor, probaby chloroiridate itself, must have been present which eliminated the induced reaction so that no further inhibition could be produced. The reaction is then not affected by the presence of small amounts of acid. The addition of a small amount of tetrachloroplatinite ions to the reaction mixture had only a small accelerating effect on the rate of the reaction in the light. The addition of excess of Cs^+ ions to this reaction mixture evidently precipitated the Pt(II) species in addition to those of Pt(IV) since the supernatant solutions were colourless. The concentration of Pt(II)–Cl bonds was therefore included in the value of the Pt–Cl bond concentrations used and the reaction would be expected to be somewhat faster merely because of the increased Pt–Cl concentration. The reaction is also sensitive to traces of thiosulphate ions. When present to about 5% of the $PtCl_6^{2-}$ concentration, 50% replacement occurred in 1 minute followed by a much slower reaction. The effect of the thiosulphate evidently overcame that of any inhibitor which was present in the sample. Qualitative experiments, in which the reaction was followed visually by observing the colour change, showed that the reaction is also accelerated by ferrous ions.

TABLE 1. *Typical results for the* $PtCl_6^{2-}$–I^- *reaction.*

$[PtCl_6^{2-}]_0 = 5{\cdot}58 \times 10^{-3}$M, $[I^-]_0 = 6{\cdot}03 \times 10^{-2}$M. Temp. = 25°.

Other conditions	Replacement (%) after (min.) 2	10	25	50	75	100	150
In light; 1×10^{-6}M-$S_2O_3^{2-}$	22·8	48·0	71·9	—	92·0	—	98·8
,, No $S_2O_3^{2-}$	25·0	48·5	69·8	85·1	92·9	96·0	—
In dark; No $S_2O_3^{2-}$	24·4	48·3	70·4	84·9	93·0	96·4	—
In light; No $S_2O_3^{2-}$; $2{\cdot}5 \times 10^{-4}$M-$IrCl_6^{2-}$ ...	24·6	47·2	69·5	84·9	95·9	97·2	—
,, No $S_2O_3^{2-}$; 5×10^{-3}M-$HClO_4$	26·0	48·3	73·0	86·2	93·5	96·9	—
,, No $S_2O_3^{2-}$; $3{\cdot}9 \times 10^{-4}$M-$PtCl_4^{2-}$ ...	31·5	57·1	79·2	92·7	97·8	102	—*

* These figures refer to uptake of iodide by both Pt(IV) and Pt(II) species.

The rate of the reaction was found to depend on the initial concentrations of both chloroplatinate and iodide ions. The second-order rate equation can be expressed in terms of the

[2] Poë and Vaidya, *J.*, 1960, 187.
[3] Poë and Vaidya, *Proc. Chem. Soc.*, 1960, 118.
[4] Poë and Vaidya, *J.*, 1960, 3431.
[5] Poë, unpublished work.

fraction, f, of the total possible reaction which has occurred by time t, and the initial concentrations of the iodide ions and Pt–Cl bonds. Thus:

$$kt = \{2{\cdot}303/([I^-]_0-[PtCl]_0)\} \log \{(1 - [PtCl]_0 f/[I^-]_0)/(1 - f)\}$$

The rate constant, k, was therefore obtained by plotting the function on the right-hand side of this equation against time. The results obtained from thirteen runs at 25° in which $[I^-]_0$ varied from 0·0214M to 0·0643M, and $[Pt–Cl]_0$ varied from 0·015M to 0·045M, were expressed graphically. A straight line was obtained, up to about 90% replacement, which did not go through the origin and which gave a rate constant of 0·9 l. mole^{-1} min.$^{-1}$. The finite value of the logarithmic term at $t = 0$ suggests some separation-induced replacement. This was confirmed by runs in which the complex was separated within about 15 sec. of mixing the reactants. The amount of replacement varied up to about 18%, but it was not constant at 17% as would have been the case if rapid replacement of one of the chloride ligands had occurred. It was not due to inadequate washing of the precipitate since the distribution of the activity after completion of the reaction was very close to that predicted from the known concentrations. Precipitation-induced reaction therefore seems most likely. The rate-constant graph can be made to go through the origin by using corrected values of the replacement obtained from the equation:

$$f_{\text{apparent}} = f_{\text{correct}} + 0{\cdot}12(1 - f_{\text{correct}})$$

based on the assumption that at any time about 12% of the reaction which has still to occur will occur during the separation process. Since only the earlier points are much affected by this, the graph is not very sensitive to the exact amount of separation-induced reaction assumed. The graph obtained is shown in the Figure. Where more than one point is available for any one time, the spread of the points is given by the length of the vertical line, where this is greater than the radius of the closed circle which indicates the average value. Single points are indicated by open circles. The gradient corresponds to a rate constant of 0·85 l. mole^{-1} min.$^{-1}$ with an uncertainty of about ±0·05 l. mole^{-1} min.$^{-1}$. Three runs, involving identical solutions, were performed at 1°, 25°, and 44° and the results are given in Table 2. The initial concentration of iodide ions was only slightly greater than that of Pt–Cl bonds, and the absolute values of the rate constants obtained were rather inaccurate since they depend partly on the difference between these concentrations. However, since the solutions were identical, and good straight-line rate-constant graphs were obtained from the data corrected for separation-induced reaction, the relative values of the rate constants were quite accurate. The value for 25° being set at 0·85 l. mole^{-1} min.$^{-1}$, the graphically obtained values for 1° and 44° are 0·111 and 3·12 l. mole^{-1} min.$^{-1}$. These results are well expressed by the equation:

$$k = (60\boldsymbol{R}Te/\boldsymbol{N}h) \exp(-26{\cdot}31/\boldsymbol{R}) \exp(-12{,}730/\boldsymbol{R}T) \text{ l. mole}^{-1} \text{ min.}^{-1},$$

which gives values of 0·114, 0·817, and 3·20 l. mole^{-1} min.$^{-1}$ for k at 1°, 25°, and 44°, respectively. Since the uncertainty in each of the values of k is not more than about ±5% the values of

TABLE 2. *Temperature dependence of the* $PtCl_6^{2-}$–I^- *reaction.*

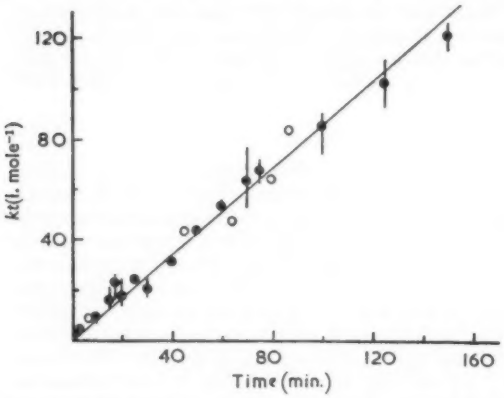
$[I^-]_0 = 3{\cdot}62 \times 10^{-2}$M; $[PtCl]_0 = 3{\cdot}35 \times 10^{-2}$M.

(The value of $[I^-]_0$–$[PtCl]_0$ is adjusted so that graphical determination gives $k_{25} = 0{\cdot}85$ mole^{-1} min.$^{-1}$. This requires a decrease of 14% in the difference, which corresponds to an uncertainty in one of the absolute values of about 1%).

25°	Time (min.)	10	25	50	75	100					
	100 $f_{corr.}$	21	39	57	68	75					
	100 $k_{calc.}$ (l. mole^{-1} min.$^{-1}$)	86	83	83	86	88					
	k_{graph} (l. mole^{-1} min.$^{-1}$)			0·85							
1°	Time (min.)	30	73	90	150	195	240	300	360	420	480
	100 $f_{corr.}$	9·3	20	28	33	41	46	51	56	58	62
	1000 $k_{calc.}$ (l. mole^{-1} min.$^{-1}$)	112	110	136	104	112	112	111	110	102	105
	k_{graph} (l. mole^{-1} min.$^{-1}$)			0·111							
44°	Time (min.)	3	6	9	11	13	15	18	20	25	30
	100 $f_{corr.}$	24	38	47	52	58	61	67	68	70	75
	100 $k_{calc.}$ (l. mole^{-1} min.$^{-1}$)	332	322	302	298	330	318	336	318	287	284
	k_{graph} (l. mole^{-1} min.$^{-1}$)	...		3·12							

E and $\Delta S^{\ddagger}$ are $12{\cdot}7_3 \pm 0{\cdot}5$ kcal./mole and $-26{\cdot}3 \pm 2$ cal./deg. mole, respectively. (These values differ from those previously quoted [3] owing to the improved treatment of the data.)

A spectrophotometric examination of equilibrium mixtures containing 0·001M-$PtHal_6^{2-}$, 0·5M-Cl^- and various small amounts of iodide showed that the intermediate species have absorptions at the same wavelengths as the hexaiodoplatinate (*i.e.*, 340, 420, and 495 mμ) but that the 420 mμ absorption is more intense than that at 495 mμ in the species containing less iodide. In the hexaiodoplatinate the absorption at 420 mμ shows only as a shoulder to the more intense absorption at 495 mμ. An examination of the changing spectrum during the reaction, in the presence of sufficient chloroiridate to minimise photochemical effects, revealed a steady growth of the hexaiodoplatinate spectrum and, therefore, no intermediate species were formed in appreciable concentrations. The straight-line rate-constant graph is obtained, therefore, because the reaction involves a rate-determining replacement of one of the chloride ligands, followed by rapid replacement of the remaining five, rather than a series



The $PtCl_6^{2-}$–I^- *reaction at 25°. A graphical representation of the rate constant data obtained from thirteen runs, involving over 70 points.*

of successive replacements governed by approximately the same rate constant and leading to a constant average value (cf. ref. 3).

The kinetics of the replacement in the presence of chloroiridate and at room temperature were examined spectrophotometrically in the presence of chloroiridate by following the changing absorption at 495 mμ. Provided the solutions were not left continuously in the light beam, linear rate-constant graphs were obtained, but the rate constants were larger than those obtained by the tracer method at corresponding ionic strengths. Thus the lowest rate constant observed at $I = 0{\cdot}05$M was 1·6 l. $mole^{-1}$ $min.^{-1}$ and we assume that this is because some extra reaction is caused by the light beam in spite of the presence of chloroiridate. On decreasing the ionic strength to 0·01M the rate constant dropped to 0·6 $mole^{-1}$ $min.^{-1}$ which is, qualitatively at least, the drop expected according to the simple Debye–Hückel equation. The difficulty in obtaining reproducible results by this method, in contrast with the good reproducibility obtained by the radiotracer method, shows that the latter is more reliable.

The $PtBr_6^{2-}$–I^- *Reaction.*—This reaction is considerably faster than that of the chloroplatinate and its study has been much less thorough. Table 3 shows most of the results in detail. The reaction is not sensitive to thiosulphate in the same way as the chloroplatinate reaction, but the runs were nevertheless performed in its absence. It is retarded a little by acid, in the light, and it is slightly photosensitive. The addition of a small amount of tetrabromoplatinate slightly accelerates the reaction in the dark over the early stages. The reaction in the dark is partially inhibited by small amounts of $IrCl_6^{2-}$, but additional quantities have no further effect and the residual reaction is presumably a genuine, non-photochemical replacement reaction.

When precipitation was effected within 15 seconds of mixing the reactants at 1°, about 17% replacement was found to have occurred. Although this corresponds closely to the fast replacement of one of the six bromide ligands, this correspondence is probably fortuitous, the rapid replacement being precipitation-induced, as in the chloroplatinate reaction. Thus, spectrophotometric observation of the reaction of 10^{-4}M-$Pt^{IV}Br_6^{2-}$ and 10^{-3}M-I^-, in the presence of

3×10^{-5}M-$IrCl_6^{2-}$ and at room temperature, shows no sudden initial increase in absorption such as would have been expected if the first stage of substitution had been rapid. Precipitation-induced reaction might be expected to occur more easily in the more labile bromoplatinate system.

The reacting solutions, in the presence of chloroiridate, showed absorption maxima at 340, 420, and 495 mμ but the 420 mμ absorption was more intense than that at 495 mμ until the later stages of the reaction: then the 495 mμ peak became more intense, as in the hexaiodoplatinate

TABLE 3. *The* $PtBr_6^{2-}$–I^- *reaction.*

	Replacement (%) after (min.)						
	½	1	1½	2½	3	7	12
(a) *At* 1°, *and* $[I^-]_0 = 9{\cdot}74 \times 10^{-3}$M, $[PtBr]_0 = 6{\cdot}12 \times 10^{-3}$M.							
In light	28·0	—	41·6	50·2	55·1	65·4	76·5
,, $PtBr_6^{2-}$ previously in dark for 24 hr.	29·8	—	40·1	50·6	55·6	68·7	77·2
In light; 10^{-3}M-$HClO_4$	20·0	—	39·7	43·7	48·3	58·4	67·2
In dark	32·7	36·0	42·2	45·9	48·4	57·7	64·1
,, $7{\cdot}7 \times 10^{-5}$M-$PtBr_4^{2-}$	35·9	41·7	45·2	—	50·7	59·9	64·8 *
,, 5×10^{-5}M-$IrCl_6^{2-}$	18·7	22·6	29·4	35·2	37·3	43·7	50·5
,, 1×10^{-4}M-$IrCl_6^{2-}$	17·2	21·5	25·7	34·6	36·7	44·0	—
(b) *At* 1°, *and* $[I^-]_0 = 7{\cdot}3 \times 10^{-3}$M, $[PtBr]_0 = 6{\cdot}12 \times 10^{-3}$M.							
In dark; 5×10^{-5}M-$IrCl_6^{2-}$	17·7	20·1	22·5	25·7	28·3	37·4	38·5
(c) *At* 25°, *and* $[I^-]_0 = 9{\cdot}74 \times 10^{-3}$M, $[PtBr]_0 = 6{\cdot}12 \times 10^{-3}$M.							
In dark; 5×10^{-5}M-$IrCl_6^{2-}$	41·8	46·6	57·2	54·7	58·3	64·5	68·8

(d) *At* 1°, *and* $[I^-]_0 = 10^{-2}$M, $[PtBr]_0 = 5{\cdot}62 \times 10^{-3}$M.

	¼	1	2	3	4 (min.)
In dark; 10^{-4}M-$IrCl_6^{2-}$	17·2	22·8	30·5	36·8	36·0
,, ,,	17·6	—	—	33·9	36·8

* These figures give the uptake of iodide by both the Pt(IV) and the Pt(II) species.

spectrum. This shows that intermediate species must be present in significant quantities, in contrast with the chloroplatinate reaction.

The rate of the reaction is dependent on the initial concentration of the iodide. After allowance for the precipitation-induced reaction as before, and with a second-order rate equation, the rate-constant plot is linear only up to a total of about 35% replacement, corresponding to the replacement of two chloride ligands, after which the gradient decreases, showing that the complexes containing more iodide react more slowly than the less substituted species. The gradient of the straight line corresponds to a rate constant of about 12 l. $mole^{-1}$ $min.^{-1}$ at 1°.

DISCUSSION

The inhibition of the $PtCl_6^{2-}$–I^- reaction by chloroiridate, and the sensitivity of the reaction to light and to traces of thiosulphate or ferrous ions, show that it can involve a labile Pt(III) intermediate in the same way as does the $PtCl_6^{2-}$–Cl^- exchange reaction.[6] The residual reaction, after addition of chloroiridate, must, however, go by some other mechanism. A redox mechanism, involving a bridged intermediate and chlorine-transfer, and similar to that proposed for the Pt $en_2Cl_2^{2+}$–Cl^- exchange,[7] would be of first order in a Pt(II) species. The small effect of adding chloroplatinate ions to the reaction mixture, and the unlikelihood of there being a substantial amount of Pt(II) in the chloroplatinate samples, make such a mechanism unlikely. The reaction is also faster than it would be if aquation were the mechanism.[3]

In the absence of evidence for yet another devious path (and previous studies of platinum complexes give little reassurance here) the second-order kinetics suggest an S_N2 mechanism. The size of the entropy of activation, and the decrease in rate with decreasing ionic strength, are both consistent with this. The only other S_N2 reactions of chloroplatinates which have been studied in detail involve the attack of neutral or

[6] Rich and Taube, *J. Amer. Chem. Soc.*, 1954, **76**, 2608.
[7] Basolo, Wilks, Pearson, and Wilkins, *J. Inorg. Nuclear Chem.*, 1958, **6**, 161.

cationic complexes by pyridine, and activation energies of about 20 kcal./mole were found.[1] The value of 12·7 kcal./mole for the $PtCl_6^{2-}$–I^- reaction, though rather small, is consistent with the greater nucleophilic character of the iodide ion and with the presumed lower strength of the Pt–Cl bond in the anionic complex. Solvation of the highly charged transition state may well help to offset the repulsion between the similarly charged reactants. The rapidity with which further replacement occurs, after the slow introduction of the first iodide ion, shows that the labilising effect of the iodide ligand, even on chloride ligands in the *cis*-positions, must be large relative to that of the chloride ligand. Although kinetically the system proceeds rapidly from $PtCl_5I^{2-}$ to PtI_6^{2-} the system at equilibrium does contain the intermediate species in significant proportions.[4]

The $PrBr_6^{2-}$–I^- reaction is partly inhibited by chloroiridate and can therefore involve a Pt(III) intermediate. The residual reaction, in the presence of chloroiridate, cannot go by this mechanism. The redox mechanism[7] involving bromoplatinite can also be rejected, and aquation is also too slow to provide a reaction path.[8] In the absence of other evidence, the second-order kinetics can be taken to indicate an S_N2 mechanism. The rate constant for replacement of the first two bromide ligands is about 100 times as great as that for the $PtCl_6^{2-}$–I^- reaction and, if the entropies of activation are similar, then the activation energy must be 2—3 kcal./mole smaller. In the reactions of the corresponding cationic complexes with pyridine the activation energy for the reaction of the bromo-complex was about 1·5 kcal./mole smaller, and the entropy of activation somewhat lower, than that for the corresponding chloro-complex.[9] A lower activation energy would parallel the weaker bond strength in the hexabromoplatinate, the Pt–Br bond being, on the average, about 6 kcal./mole weaker than the Pt–Cl bond.[10] On going to the iodoplatinate exchange reaction, a further increase in the rate constant by a similar amount would result in a value of 10^3 l. $mole^{-1}$ $min.^{-1}$. This would give a half-time for exchange of about 8 seconds in the most dilute solutions studied.[2] This would hardly have been detectable, with the technique used, especially if there were an appreciable amount of precipitation-induced exchange. Although it is possible that the rapid and complete exchange observed was entirely precipitation-induced this would be an alternative manifestation of the increasing lability along the series chloro-, bromo-, and iodo-platinate. The slow replacement of the third and subsequent bromide ligands, compared with the replacement of the first two, is in contrast with the increased rate observed with the chloroplatinate. A similar contrast exists in the replacement equilibria for which the average spreading factors[11] in the chloride–iodide and bromide–iodide systems are 0·9 and 1·1, respectively.[4]

The observations on the reactions which apparently involve Pt(III) intermediates can be considered together with some results for the $PtCl_6^{2-}$–Cl^- exchange reaction[12] which differ from those reported by Rich and Taube.[6] Sodium hexachloroplatinate was used which had been shown spectrographically to contain less than 5×10^{-4} % of iridium. This underwent relatively slow exchange with chloride, and half times of about 2½ hr. were obtained at 25° in the light. With sodium chloroplatinate, of normal grade rapid exchange was induced by addition of less than 1% of thiosulphate ions, relative to the chloroplatinate. These results suggest that laboratory light is a relatively poor generator of Pt(III) species compared with chemical, one-electron, reducing agents but that, when generated, these species provide a path for rapid exchange or replacement reactions. Ions such as PtI_5^{2-} must, therefore, be capable of extracting chlorine or bromine atoms rapidly from $PtCl_6^{2-}$ or $PtBr_6^{2-}$, thereby propagating the reaction by regeneration of $PtCl_5^{2-}$ or $PtBr_5^{2-}$.

[8] Archibald, *J.*, 1920, **117**, 1104; 1922, **121**, 2849.
[9] Grinberg, *J. Inorg. Chem.* (*U.S.S.R.*), 1959, **4**, 683.
[10] Poë and Vaidya, *J.*, 1961, 1023.
[11] Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1957.
[12] Burford and Poë, unpublished work.

Experimental

The radiotracer procedures were those used in the study of the PtI_6^{2-}–I^- exchange reaction.[2] The agreement between the total activity added and the sum of activities in the free and combined iodide, measured after replacement, was usually within ±1—2%. Sufficient activity was used to keep statistical uncertainties below ±1%. Platinum complexes were supplied by Messrs. Johnson, Matthey and Co. Ltd. and "AnalaR" halide salts were used.

A Perkin–Elmer recording spectrophotometer (model 4000) was used to study the changing spectra during the reactions, and changing absorption at a single wavelength was measured on a Unicam S.P. 500 spectrophotometer.

We are grateful to Messrs. Johnson, Matthey and Co. Ltd. for the loan of the spectrographically analysed sodium hexachloroplatinate.

Inorganic Chemistry Research Laboratories,
Imperial College, London, S.W.7. [*Received, January 19th*, 1961.]

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573. *The Reaction of Uranium with Solutions of Alkylammonium Nitrates in Dinitrogen Tetroxide; Some Properties of Alkylammonium Uranyl Nitrates.*

By C. C. Addison and N. Hodge.

The reaction of metallic uranium, or uranium oxides, with solutions of alkylammonium nitrates in liquid dinitrogen tetroxide is a satisfactory and rapid method for the preparation of alkylammonium uranyl nitrates $UO_2(NO_3)_2,MNO_3$ or $UO_2(NO_3)_2,2MNO_3$ (where M is $EtNH_3$, Et_2NH_2, Et_3NH, or Et_4N). With ethylammonium nitrate, both compounds can be prepared. With di- and tri-ethylammonium nitrate only the 1 : 1 compound is isolated; a mixture of the two compounds is obtained with tetraethylammonium nitrate. In the reactions with metallic uranium, uranium(IV) compounds are formed as intermediates and have a greater stability in these solutions than in dinitrogen tetroxide alone. Solutions of the 1 : 1 compounds in nitromethane have been studied by the methods of electrolysis, conductometric titration, light absorption, molecular weight, and ultraviolet spectra, and shown to contain the $[UO_2(NO_3)_3]^-$ ion. Solutions of the 1 : 2 compounds also contain this anion, and no evidence has been found for the existence of the ion $[UO_2(NO_3)_4]^{2-}$ in non-aqueous solvents. Some rates of reaction of uranium with alkylammonium nitrate solutions are recorded.

Uranyl nitrate combines with various other nitrates to give double salts which may contain the trinitrato- and the tetranitrato-uranyl complex anions $[UO_2(NO_3)_3]^-$ and $[UO_2(NO_3)_4]^{2-}$. These anions have been of interest in recent years because they represent one type of species involved in the solvent-extraction of uranium compounds, and because similar complexes are formed by some transuranium elements. The identity of the trinitratouranyl ion has been established with much greater certainty than that of the tetranitratouranyl ion. Compounds of general formula $M[UO_2(NO_3)_3]$ (where M = NH_4, K, Rb, or Cs) are known,[1,2] and an *X*-ray study of the rubidium salt leaves no doubt that the anion exists as a separate entity.[3] The anion has also been recognised in solution, by spectrophotometric study of solutions of uranyl nitrate in acetone containing tetrabutylammonium nitrate.[4] The salt $NMe_4[UO_2(NO_3)_3]$ has been crystallised from solutions of the appropriate nitrates in pure nitric acid.[5] In contrast, the existence of the tetranitratouranyl ion appears to have been deduced only from the stoicheiometry of double

[1] Rimbach, *Ber.*, 1904, **37**, 461.
[2] Dieke and Duncan, "Spectroscopic Properties of Uranium Compounds," McGraw-Hill, New York, 1949, p. 138.
[3] Ref. 2, pp. 13 *et seq.*
[4] Kaplan, Hildebrandt, and Ader, *J. Inorg. Nuclear Chem.*, 1956, **2**, 153.
[5] Jander and Wendt, *Z. anorg. Chem.*, 1949, **258**, 1.

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salts. Compounds of formula $M_2[UO_2(NO_3)_4]$ (where M = K,[6] NH_4,[6] NEt_4,[7] or NMe_4 [7]) have been described, but there is little evidence for the identity of such an anion.

Preparation of these compounds has often involved reactions in concentrated nitric acid. In these, and in the study of the complexes by extraction methods, water is inevitably present, and the chemical behaviour of both simple and complex nitrates is therefore restricted. Liquid dinitrogen tetroxide, however, is an excellent medium for the preparation of these compounds in pure, anhydrous form. The alkylammonium nitrates are formally basic in the dinitrogen tetroxide solvent system; uranium reacts rapidly with solutions of the alkylammonium nitrates, and alkylammonium uranyl nitrates can be crystallised readily from the solutions.

These compounds were studied for two main reasons. First, by using ethylammonium nitrate solutions it is possible to crystallise either the trinitrato- or the tetranitrato-uranyl compound. No complications then arise from the use of different cations or methods of preparation, and the properties of the two compounds, and their solutions in non-aqueous solvents, can be compared directly. Secondly, the study of these double salts in non-aqueous solvents involves the use of anhydrous uranyl nitrate, the existence of which has been subject to some doubt. We have now been able to prepare this compound in pure form by careful thermal decomposition of the addition compound $UO_2(NO_3)_2,N_2O_4$. It has a high solubility in a number of polar solvents such as nitromethane, and its association with the nitrate ion could therefore be studied by conductimetric and spectroscopic techniques.

Results and Discussion

Ethylammonium Nitrate Solutions.—Solutions containing up to 58 wt. % of the nitrate in dinitrogen tetroxide separate immediately at room temperature into two layers. The upper layer contains the nitrate, the lower layer being almost pure tetroxide. For the preparation of the trinitratouranyl compound, dilute (10—20%) solutions were used. Uranium reacts readily on immersion in the upper layer; the product is concentrated in this layer, which increases in volume. Eventually the density of this layer exceeds that of dinitrogen tetroxide, and inversion occurs. The compound $(EtNH_3)[UO_2(NO_3)_3]$ separates from the lower layer as clear, yellow-green crystals.

Solutions containing more than 58% of ethylammonium nitrate are homogeneous. Reaction of these concentrated solutions with uranium is again rapid, and the analysis of the crystals which separate from this medium corresponds with the formula $(EtNH_3)_2[UO_2(NO_3)_4]$. The overall reactions are represented by the schemes:

$$U + EtNH_3NO_3 + 3N_2O_4 \longrightarrow (EtNH_3)[UO_2(NO_3)_3] + 4NO$$
$$(EtNH_3)[UO_2(NO_3)_3] + EtNH_3NO_3 \longrightarrow (EtNH_3)_2[UO_2(NO_3)_4]$$

Di- and Tri-ethylammonium Nitrate Solutions.—Solutions of these two nitrates behave similarly. Each nitrate gives a homogeneous solution in dinitrogen tetroxide at all concentrations, but separation into two phases occurs on solution of a third component, *e.g.*, a metal salt. As uranium reacted with a 10—20% solution, an immiscible liquid was formed at the metal surface, which rose as globules to form an upper liquid phase. As reaction proceeded, this layer increased in volume and density until inversion of the two layers occurred. From the lower layer the compounds $(Et_2NH_2)[UO_2(NO_3)_3]$ or $(Et_3NH)[UO_2(NO_3)_3]$ crystallised in pure form. Attempts to prepare the tetranitrato-uranyl compounds by the use of high alkylammonium nitrate concentrations gave only viscous yellow solutions which could not be induced to crystallise.

Tetraethylammonium Nitrate Solutions.—Tetramethyl- and tetraethyl-ammonium nitrate are only slightly soluble in dinitrogen tetroxide. Reaction of uranium with the relatively dilute solutions available is slow; and the product is also insoluble, which further inhibits reaction. When tetraethylammonium nitrate was used, analysis indicated

[6] " Fluorescence of the Uranyl Salts," Carnegie Inst. Wash. Pub., Washington D.C. 1919, p. 208.
[7] Ref. 2, pp. 139, 140.

that the product was a mixture of $(Et_4N)[UO_2(NO_3)_3]$ and $(Et_4N)_2[UO_2(NO_3)_4]$, but in no case was either compound isolated in the pure state. Absolute nitric acid is probably a better medium for the preparation of the tetra-alkylammonium salts.[5]

Reaction of Uranium Oxides.—Whereas the oxides UO_3 and U_3O_8 do not react with liquid dinitrogen tetroxide at ordinary temperatures and pressures, they are readily dissolved by solutions of mono-, di-, and tri-ethylammonium nitrate, to yield the same products as described above.

Presence of U(IV) *in Alkylammonium Nitrate Solutions.*—In solutions which contain no strongly co-ordinating groups (*e.g.*, $NOCl$–N_2O_4 mixtures [8]) any oxidation state of uranium lower than U(VI) has only transitory existence. However, during the reaction of uranium metal with alkylammonium nitrate solutions, much quadrivalent uranium was present in the solutions, although efforts to isolate solid uranium(IV) compounds were unsuccessful. The presence of uranium(IV) gave to the solutions a brown colour which was quite different from that produced by dinitrogen trioxide or the uranyl compounds and persisted for some time after the removal of the metal from the solution. The presence of uranium(IV) was also shown by dropping a portion of the solution into dilute aqueous ammonia; grey-green UO_2,xH_2O was formed which could be separated, acidified, and titrated with potassium permanganate. Although the solutions were not examined quantitatively at this intermediate stage, the following general observations were made: (*a*) The greater the concentration of alkylammonium nitrate, the more uranium(IV) was present in solution for equivalent reaction times. This suggests the stabilisation of the U(IV) state by nitrate co-ordination, probably as the $[U(NO_3)_6]^{2-}$ ion. Neither this ion nor the simple uranium tetranitrate has been described, but corresponding compounds of plutonium (for which the quadrivalent state is more stable), *i.e.*, $K_2[Pu(NO_3)_6]$ [9] and $Pu(NO_3)_4,5H_2O$,[10] are well known. (*b*) The quantity of uranium(IV) in the solution varied with the cation present, in the increasing order $EtNH_3^+$, $Et_2NH_2^+$, Et_3NH^+, Et_4N^+. This is the reverse of the order in which these ions show hydrogen-bonding to the nitrate ion, and the quantity of uranium(IV) in solution therefore increases with increasing availability of the nitrate ions for co-ordination to the U(IV) ion.

It appears, then, that the optimum conditions for the preparation of salts of the $[U(NO_3)_6]^{2-}$ ion involve the use of high concentrations of tetraethylammonium nitrate, for which concentrated nitric acid is a better reaction medium than dinitrogen tetroxide.

Ionisation of Diethylammonium Uranyl Trinitrate.—Possible modes of ionisation of this typical compound are as follows:

$$(Et_2NH_2)[UO_2(NO_3)_3] \rightleftharpoons Et_2NH_2^+ + [UO_2(NO_3)_3]^- \quad (1)$$

$$\rightleftharpoons Et_2NH_2^+ + UO_2(NO_3)_2 + NO_3^- \quad (2)$$

$$\rightleftharpoons Et_2NH_2^+ + UO_2NO_3^+ + 2NO_3^- \quad (3)$$

$$\rightleftharpoons Et_2NH_2^+ + UO_2^{2+} + 3NO_3^- \quad (4)$$

In aqueous solution, ionic dissociation occurs; on electrolysis, uranium migrates to the cathode and is present in cationic form (equations 3 or 4). The compound is highly soluble in nitrobenzene ($\varepsilon = 35$). On electrolysis of a 0·067M-solution at 230 v and 20°, uranium became concentrated in the anode compartment, indicating the presence of the $[UO_2(NO_3)_3]^-$ ion in nitrobenzene (equation 1). Further information on the species present in very dilute solutions was obtained from cryoscopic molecular-weight measurements (Table 1). It is clear that at all higher concentrations the molecule dissociates into two ions only (equation 1), and that the trinitratouranyl ion undergoes further dissociation only at very high dilution.

Conductivity Measurements.—By using solutions of anhydrous uranyl nitrate in

[8] Addison and Hodge, *J.*, 1961, 2490.
[9] Cunningham, "The Actinide Elements," Nat. Nuclear Energy Ser. Div. (IV), 1954, chapter 10, p. 371.
[10] Drummond and Welch, *J.*, 1956, 2565.

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TABLE 1. *Dissociation of diethylammonium uranyl trinitrate in nitrobenzene.*

Molar concn.	0·0022	0·0068	0·0115	0·155
ΔT_f	0·044°	0·107°	0·158°	0·192°
Mean mol. wt.	155	193	220	245
Particles produced per mole of solute	3·42	2·75	2·41	2·16

nitromethane, it has been possible to study the formation of nitratouranyl ions in non-aqueous media. A solution of 0·141 g. of anhydrous uranyl nitrate in 10 ml. of nitromethane was titrated conductometrically with a 0·168M-solution of ethylammonium nitrate in nitromethane (Fig. 1). The initial very low conductivity of uranyl nitrate increases rapidly on addition of ethylammonium nitrate until the 1 : 1 ratio is achieved in

FIG. 1. *Conductometric titration of anhydrous uranyl nitrate with ethylammonium nitrate in nitromethane.*

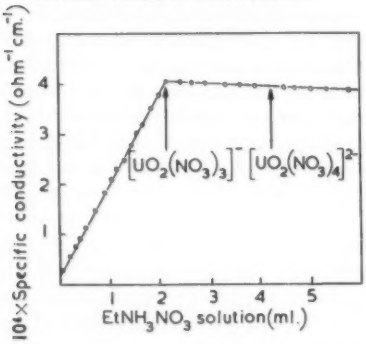
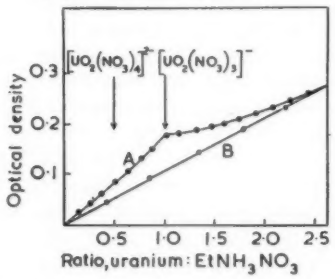


FIG. 2. *Variation in light absorption by a solution of anhydrous uranyl nitrate* (A) *in nitromethane on dilution with a solution of ethylammonium nitrate in nitromethane and* (B) *in nitromethane alone.*



solution. Thereafter conductivity falls slightly and there is no further break, so that the ionic dissociation

$$(EtNH_3)[UO_2(NO_3)_3] \longrightarrow EtNH_3^+ + [UO_2(NO_3)_3]^-$$

makes a much greater contribution to the total conductivity in nitromethane than does the ionic dissociation of uranyl nitrate or ethylammonium nitrate. The arrows (Fig. 1) indicate 1 : 1 and 2 : 1 molar ratios; the results provide convincing evidence (*a*) that the ion $[UO_2(NO_3)_3]^-$ has a high stability in nitromethane, and (*b*) that the ion $[UO_2(NO_3)_4]^{2-}$ does not exist in solution, even though a compound of empirical formula $UO_2(NO_3)_2,2EtNH_3NO_3$ can be obtained crystalline.

Light Absorption Measurements.—The above observations were confirmed during a study of the applicability of Beer's law to these solutions. The light transmitted in a Hilger " Spekker " absorptiometer when a 0·084M-solution of anhydrous uranyl nitrate in nitromethane was diluted with nitromethane obeys Beer's law (line B, Fig. 2). When a solution of ethylammonium nitrate in nitromethane was used as diluent (curve A, Fig. 2) optical density is not proportional to concentration; a single sharp break occurs at the 1 : 1 ratio, but there is again no evidence for the $[UO_2(NO_3)_4]^{2-}$ ion.

Conductivity and light-absorption measurements similar to those described above have been carried out with di-, tri- and tetra-ethylammonium nitrates also, and the results are similar.

Ultraviolet Absorption Spectra.—Solutions of mono-, di-, or tri-ethylammonium uranyl trinitrate in nitromethane give almost identical ultraviolet spectra, which are shown as the full line in Fig. 3. The spectrum consists of a series of bands spaced regularly 14 mμ apart, which are characteristic of the excited electronic states of the uranyl group. The three bands at 440, 454, and 468 mμ are the most pronounced and the most important when complex-formation by the uranyl group is being considered. When the uranyl ion becomes part of a nitrato-complex ion, the interaction of nitrate ions with the uranyl ion leads to

enhanced absorption at these wavelengths, and these spectra therefore provide a useful means of showing the presence of complex ions. This is illustrated in Fig. 3 by the spectrum of the compound $UO_2(NO_3)_2,N_2O_4$, shown as a broken line. The chemistry of solutions of this compound (which will be discussed in detail together with that of the

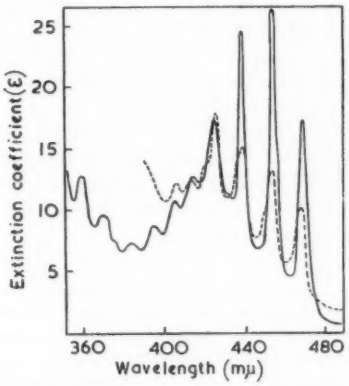


FIG. 3. *Ultraviolet absorption spectra of nitromethane solutions.*

Full line: $(EtNH_3)[UO_2(NO_3)_3]$, $(Et_2NH_2)[UO_2(NO_3)_3]$, and $(Et_3NH)[UO_2(NO_3)_3]$.

Broken line: $UO_2(NO_3)_2,N_2O_4$.

anhydrous nitrate in a later paper) indicates that $[UO_2(NO_3)_3]^-$ ions are not present to any appreciable extent. When alkylammonium nitrate is added to the solution, there is immediate enhancement of the absorption at the three higher wavelengths. Characteristics of the spectrum for each of the compounds studied are collected in Table 2. The spectra of the first three compounds are quite consistent with the simple dissociation to

TABLE 2. *Ultraviolet absorption spectra of solutions of alkylammonium uranyl nitrates in nitromethane.*

Compound	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
$EtNH_3[UO_2(NO_3)_3]$	425	17·6	440	25·0	455	26·8	468	18·3
$Et_2NH_2[UO_2(NO_3)_3]$	426	17·3	440	24·5	455	27·0	469	17·3
$Et_3NH[UO_2(NO_3)_3]$	426	17·4	440	25·0	454	27·1	468	17·9
$(EtNH_3)_2[UO_2(NO_3)_4]$	425	17·7	439	25·3	455	27·0	469	17·9
$UO_2(NO_3)_2,N_2O_4$	427	16·3	438	15·2	454	13·8	468	10·8

alkylammonium and trinitrato-uranyl ions. The striking observation is that the spectrum of ethylammonium uranyl tetranitrate is virtually identical with the spectra of the compounds in which the presence of the trinitratouranyl ion can be accepted. Since the co-ordination of one NO_3^- ion to the $UO_2(NO_3)_2$ molecule brings about such a pronounced enhancement of the " uranyl " peaks, it would be expected that the co-ordination of a second NO_3^- ion would also be reflected in the spectrum. We therefore believe that this compound ionises in nitromethane as follows:

$$(EtNH_3)_2[UO_2(NO_3)_4] \longrightarrow 2EtNH_3^+ + [UO_2(NO_3)_3]^- + NO_3^-$$

and that even if the complex ion $[UO_2(NO_3)_4]^{2-}$ exists in the solid state (which must now be regarded as doubtful) there is no evidence for its existence in solution.

The apparent upper limit of three nitrate ions in a uranyl complex is not set by the nitrate ions, since the existence of the tetranitratozincate ion, for example, has been established [11] for nitromethane solutions. It is presumably a consequence of the peculiar stability of the $[UO_2(NO_3)_3]^-$ ion. From an *X*-ray study of the rubidium salt,[3] each nitrate ion is believed to be bidentate, and the uranium atom is then surrounded by a ring of six oxygen atoms in a plane at right angles to the uranyl group. This structure is believed to occur in the uranyl nitrate hydrates also.[12]

Nitromethane was selected as solvent in these experiments because the solutions are

[11] Addison and Hodge, *J.*, 1954, 1138.
[12] Gatehouse and Comyns, *J.*, 1958, 3965.

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stable. Solutions in other non-aqueous solvents give closely similar spectra. For example, fresh solutions in cyclohexanone are bright yellow and their spectra resemble those in Fig. 3, but the solutions darken rapidly owing to oxidation of the solvent.

Other Properties of Diethylammonium Uranyl Trinitrate.—The crystals are bright yellow and very deliquescent. They show only weak fluorescence to ultraviolet radiation. [Anhydrous uranyl nitrate is also weakly fluorescent, whereas the compound $UO_2(NO_3)_2,N_2O_4$ and the uranyl nitrate hydrates are strongly fluorescent.] The compound did not dissolve in, or react with, ether, benzene, carbon tetrachloride, or dioxan.

The compound melted sharply at 115° to a clear yellow liquid. On further heating, no change occurred until 166°, when diethylnitrosamine and nitric acid were identified in the evolved gases. Loss in weight at this temperature was only 1·2% per hour, and 2·1% per hour at 173°. At 176°, violent decomposition occurred, leaving a residue of uranium trioxide. This decomposition at a critical temperature was typical of all the alkylammonium uranyl nitrates.

Experimental

Alkylammonium nitrates were prepared by solvolysis of the chlorides in dinitrogen tetroxide, as already described for $EtNH_3NO_3$,[11] $Et_2NH_2NO_3$,[13] and Et_3NHNO_3.[14] The alkylammonium uranyl nitrates were separated from mother-liquor by washing them with nitromethane and dinitrogen tetroxide. Ethylammonium uranyl tetranitrate could not be treated in this way, being highly soluble in both solvents. This compound was given prolonged filtration on a sintered-glass plate in an argon atmosphere. The products were analysed by distilling the amine constituent into standard acid. Nitrate was determined in the residue by the Kjeldahl method. Uranium was precipitated as ammonium diuranate and ignited to U_3O_8 (Table 3).

Molecular-weight determinations were carried out in conventional apparatus with purified nitrobenzene (m. p. 5·75°). Results in Table 1 were calculated by assuming a molar depression constant of 6·89.[15]

Conductivity measurements were carried out in an apparatus similar to that already described.[16]

Ultraviolet absorption spectra were measured by using a Unicam S.P. 500 spectrophotometer, with fused silica cells, at a temperature close to 20°.

Table 3. *Analysis of alkylammonium uranyl nitrates.*

	Required (%)			Found (%)		
	$[R_4N]$	U	NO_3	$[R_4N]$	U	NO_3
$(EtNH_3)[UO_2(NO_3)_3]$	9·2	47·4	37·0	9·3	47·6	36·2
$(EtNH_3)_2[UO_2(NO_3)_4]$	15·1	39·0	40·6	15·9	39·0	39·8
$(Et_2NH_2)[UO_2(NO_3)_3]$	14·0	44·9	35·1	14·2	44·7	35·2
$(Et_2NH)[UO_2(NO_3)_3]$	18·3	42·5	33·3	18·6	42·4	34·0

Rates of Reaction of Uranium.—Rates of reaction with three solutions of diethylammonium nitrate in dinitrogen tetroxide are compared in Fig. 4 with corresponding rates of reaction in nitromethane–dinitrogen tetroxide mixtures. Uranium discs were rotated in the solutions at 20°, at a speed of 350 r.p.m., as described elsewhere.[17] The rate of solution of uranium is constant during the first 6 hours' immersion and varies only slightly on longer immersion.

Where metal–dinitrogen tetroxide reactions are brought about by the introduction of a third component, rates of reaction vary widely with composition of the solution.[17] This is illustrated by curves (d) and (e) of Fig. 4. With the diethylammonium nitrate solutions, however, reaction rates are almost independent of concentration. Furthermore, solutions of the mono-, tri-, and tetra-ethylammonium nitrate of various concentrations also gave results lying very close to curves (a), (b), and (c), Fig. 4. In all alkylammonium nitrate solutions the reactive species is considered [17] to be the complex ion $[R_3N \longrightarrow NO^+]$ where R = H or Et, and reaction rate should be highly concentration-dependent. To explain the apparent anomaly, the influence of dinitrogen trioxide and of stirring rate was therefore examined.

[13] Addison, Conduit, and Thompson, *J.*, 1951, 1298.
[14] Addison and Hodge, *Chem. and Ind.*, 1953, 1315.
[15] Roberts and Bury, *J.*, 1923, 2037.
[16] Addison, Hodge, and Lewis, *J.*, 1953, 2631.
[17] Addison, Sheldon, and Hodge, *J.*, 1956, 3900.

TABLE 4. *Influence of* N_2O_3 *on the* $U-N_2O_4$ *reaction.*

Wt. % of N_2O_3 in N_2O_4	U * dissolved	Wt. % of mixture (col. 1) in $MeNO_2$	U * dissolved	U * dissolved in corresponding $MeNO_2$–N_2O_4 mixture
2·10	0·0	28·7	1·79	1·80
4·00	0·01	30·8	1·89	1·90
5·15	0·03	31·6	1·93	1·93
10·0	0·10	—	—	—
16·0	0·22	—	—	—

* Units are mg./cm.²/2 hr.

(a) *Influence of dinitrogen trioxide.* Some of the nitric oxide formed in the reaction of uranium with these solutions dissolves to give dinitrogen trioxide. Since this is known [18] to increase the reaction rate of zinc with dinitrogen tetroxide, it was necessary to determine the extent to which it might also enhance a uranium–dinitrogen tetroxide reaction. The results are

FIG. 4. *Rates of reaction of uranium with liquid dinitrogen tetroxide containing*: (a) 0·084M-$Et_2NH_2NO_3$, (b) 0·052M-$Et_2NH_2NO_3$, (c) 0·027M-$Et_2NH_2NO_3$, (d) 0·86M-$MeNO_2$, (e) 0·072M-$MeNO_2$.

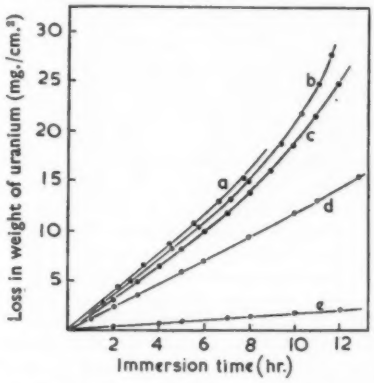
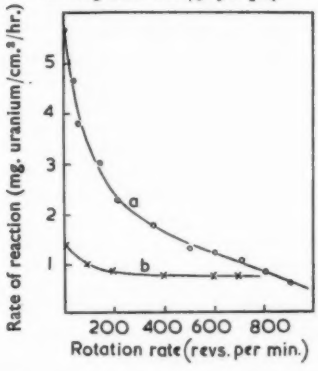


FIG. 5. *Influence of stirring rate on reaction of uranium with* (a) 0·052M-*solution* of $Et_2NH_2NO_3$ *in liquid dinitrogen tetroxide and* (b) $MeNO_2$–N_2O_4 *mixture containing* 35·3 wt. % *of* N_2O_4.



given in Table 4. Uranium discs were rotated at 350 r.p.m. and 0° in N_2O_3–N_2O_4 mixtures (column 1). At high N_2O_3 concentrations, the solution rate becomes appreciable. However, in the alkylammonium nitrate solutions the trioxide concentration is less than 5%, and hence has a negligible effect on the solution rate of uranium. The solutions in column (1) were diluted with nitromethane, and the values given in column (3) represent the total wt. % of nitrogen oxides in nitromethane. The rate of reaction of uranium with these solutions (column 4) is the same as with corresponding solutions containing dinitrogen tetroxide only (column 5). The trioxide influences reaction rates by increasing the dielectric constant of the medium (and thus the N_2O_4 self-ionisation) and, when nitromethane or other polar substance is already present, the influence of dinitrogen trioxide is negligible.

(b) *Influence of stirring rate.* Rates of reaction were determined in a diethylammonium nitrate solution at 20°, at various rotation speeds, and the results are shown in Fig. 5. The reaction rate falls continuously with increasing rotation speed, and approaches zero as rotation rates reach 1000 r.p.m. This variation is much more pronounced than in any other metal–dinitrogen tetroxide system studied.[17] The results are compared in Fig. 5 with those for a nitromethane–dinitrogen tetroxide solution. In the latter case, reaction rate is independent of stirring at speeds above 350 r.p.m.; the uranium surface is in contact with a homogeneous solution, and reaction rate is dependent only on desorption of metal ions from the surface. The results with diethylammonium nitrate solutions are interpreted satisfactorily on the basis of the two liquid phases present in the system. On initial immersion, the whole of the uranium surface is in contact with a homogeneous solution. When small amounts of uranium salts

[18] Addison, Lewis, and Thompson, *J.*, 1951, 2838.

enter the liquid, two phases are formed (which will be present as an emulsion in these experiments). The phase which contains almost all the alkylammonium nitrate tends to adhere to the metal surface, and reaction rates are therefore high in unstirred systems. This phase is removed from the surface by stirring, and the surface is then brought into contact (to an extent which depends on rotation rate) with the second liquid phase which consists of almost pure dinitrogen tetroxide. Uranium does not react with this phase, and the results in Fig. 5 therefore reflect the difference in the reactivity of uranium with the two phases. The rate of reaction of uranium with these solutions is therefore determined more by stirring rate than by solute concentration, which accounts for the very small concentration effect noted in Fig. 4.

THE UNIVERSITY, NOTTINGHAM. [*Received, January 20th*, 1961.]

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574. *Thermochemical Studies. Part IV.*[1] *Heats and Entropies of Reaction of Transition-metal Ions with Diethylenetriamine.*

By M. CIAMPOLINI, P. PAOLETTI, and L. SACCONI.

Values (valid for solutions in 0·1M-potassium chloride at 25°) for the heats of formation of successive step-complexes of Mn(II), Fe(II), Co(II), Ni(II), Cu(II), and Zn(II) with diethylenetriamine have been measured calorimetrically. These values have then been used for calculating the corresponding entropy changes. The enthalpy changes in the formation of metal complexes with two molecules of diethylenetriamine are generally less negative by 3—4 kcal. mole^{-1} than those for the corresponding trisethylenediamine complexes. The favourable entropy factor, however, gives these complexes stabilities practically equal to those of the trisethylenediamine complex ions. For each metal, with the exception of copper, the value of ΔH_2 is more negative than that of ΔH_1. The small negative value of ΔH_1 for the species $[Zn\ den]^{2+}$ is ascribed to the formation of a tetrahedral complex, a hypothesis which is supported by the exceptionally large entropy term $\Delta S_1 = +18{\cdot}5$ cal. degree^{-1} mole^{-1}.

IN a previous determination of the heats of formation of the complex ions of ethylenediamine with manganese(II), iron(II), cobalt(II), nickel(II), and zinc(II) in M-potassium chloride,[1] it was found that the values of ΔH_{1-3}, corrected for the crystal-field stabilisation energy and plotted against atomic number, increased monotonically from manganese to zinc and lay on a curve above the straight line manganese–zinc.

To extend these results, the heats of formation of analogous complexes of diethylenetriamine, $NH(CH_2{\cdot}CH_2{\cdot}NH_2)_2$, with the transition ions from manganese to zinc have been measured by a direct calorimetric method. The visible spectra were also investigated in order to determine the value of Dq needed to calculate the crystal-field stabilisation energy.

Since the values of the equilibrium constants of most of these ions reported in the literature [2] had been determined in 0·1M-potassium chloride, this ionic medium was chosen for the measurements. It has the advantage over M-potassium chloride that complications due to the formation of chloro-complexes are avoided. Since it is a tridentate ligand, diethylenetriamine enables the influence of chelation on the stability of the complexes to be studied.

Incomplete data on the enthalpy of formation of metal complexes with diethylenetriamine are recorded in the literature.[3,4] These are, however, not completely reliable since they were determined, not by a direct calorimetric method, but by measuring the temperature coefficient of the equilibrium constant.

[1] Part III, Ciampolini, Paoletti, and Sacconi, *J.*, 1960, 4553.
[2] Prue and Schwarzenbach, *Helv. Chim. Acta*, 1950, **33**, 985.
[3] Jonassen, Hurst, LeBlanc, and Meibohm, *J. Phys. Chem.*, 1952, **56**, 16.
[4] McIntyre, jun., Block, and Fernelius, *J. Amer. Chem. Soc.*, 1959, **81**, 529.

Experimental

Materials.—Diethylenetriamine (den) was distilled twice through a Todd column. The cut used (n_D^{25} 1·4815; d_4^{25} 0·9456) was titrated potentiometrically against hydrochloric acid and found to be 99·6% pure. This base was dissolved in a carbon dioxide-free 0·1M-potassium chloride and its concentration determined potentiometrically against hydrochloric acid.

The solutions of reagent-grade manganous, cobaltous, nickel, copper and zinc sulphates were about 0·4M. Manganese was determined by potentiometric titration with a standard solution of potassium permanganate, cobalt and zinc gravimetrically as anthranilates, nickel with dimethylglyoxime, and copper by electrodeposition. The ferrous sulphate solution was roughly molar with respect to the metal salt and 0·015N with respect to the hydrochloric acid. Its preparation and mode of preservation are described elsewhere.[1] Nitrogen and hydrogen were purified by being passed through copper gauze at 400°.

Calorimetric Measurements.—The calorimeter used to measure the heats of reaction between diethylenetriamine and the metal ions was the same as that described for the measurements of the heat of formation of the ethylenediamine complexes,[1] and the same experimental procedure was adopted. With copper, buffering was necessary to avoid the formation of the complex ion [Cu den(OH)]$^+$. This was done by placing in the Dewar vessel the proper amount of *ca.* 1·5N-hydrochloric acid (see Table 1, column 3). Distilled water necessary to give an ionic strength of 0·1 was added and the volume made up to about 930 ml. with 0·1M-potassium chloride.

Spectrophotometric Measurements.—The spectra of the complexes [Fe den_2]$^{2+}$, [Co den_3]$^{2+}$, [Ni den_2]$^{2+}$ were measured with a Beckman DU spectrophotometer with 1 cm. stoppered silica cells. The spectrum of the nickel complex has already been recorded [5] and our results are in good agreement. The oxidisable solution containing the complex ion [Fe den_2]$^{2+}$ was prepared and transferred to the cell in the manner already described [1] for the preparation of solutions of [Fe en_3]$^{2+}$. The solution of bisdiethylenetriaminecobalt(II) was prepared, as well as transferred to the cell, under nitrogen. The solutions of the metal chlorides were 0·4M for iron and cobalt and 0·06M for nickel. The concentration of free base (always present in excess) was 0·4M in every case.

Results

The calorimetric data are shown in Table 1. The distribution of ionic species present in the various systems before and after the reaction was calculated by using the known values of the stability constants determined in 0·1M-potassium chloride,[2] and correcting these to 25° with the values of ΔH obtained in this work. The heat evolved was corrected for the thermal effect arising from the side reaction in unbuffered systems:

$$\text{den H}^+ + \text{OH}^- \rightleftharpoons \text{den} + \text{H}_2\text{O} \qquad \Delta H = -2600 \text{ cal. mole}^{-1}$$

With buffered systems containing iron- and copper-diethylenetriamine, changes in the concentration of the various protonated forms of the base were taken into account in calculating the heat of reaction. For this purpose previously determined values of the molar heat of neutralisation were used.[6] Column 5 of Table 1 gives the heat (Q) evolved in each experiment, corrected for the heat of dilution of the metal salt. The heat effects due to the reactions which take place in buffered or in unbuffered systems are reported in column 6. The last column gives the values of ΔH_a, the average heat of reaction per mole of diethylenetriamine bound to the metal ion. The values of ΔH_a for adjacent values of $\bar{n}$ ($\bar{n}$ = average number of ligands attached to one metal ion) give an indication of the reproducibility of the measurements.

The heat of stepwise complex-formation for the separate complexes was obtained by combining the results of two runs carried out at different $\bar{n}$ and solving the set of two simultaneous equations:

$$Q_m = \alpha_1 \Delta H_1 + \alpha_2 \Delta H_{1-2}$$

where Q_m is the heat evolved per g.-ion of metal added and α_1, α_2 are the degrees of formation of the two complexes in the reaction mixture.

The estimated errors are: $\pm$200 cal. mole^{-1} for ΔH_1 and $\pm$100 cal. mole^{-1} for ΔH_{1-2}.

Table 2 shows the values of the thermodynamic functions ΔG, ΔH, and ΔS of the two

[5] Jörgensen, *Acta Chem. Scand.*, 1956, **10**, 887.
[6] Unpublished results.

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TABLE 1. *Systems* MSO_4 + den *in* 0·1M-*potassium chloride.*

Metal	Metal (10^{-5} mole)	HCl (10^{-5} mole)	den (10^{-5} mole)	Q (cal.)	Q_{ex} (cal.)	$\bar{n}$	$-\Delta H_s$ (kcal. mole^{-1})
Mn^{2+} (932 ml.)	930		28,600	65·0	0	2·00	3·5
	930		31,100	64·0	0	2·00	3·4
	888		31,700	61·6	0	2·00	3·5
	915		31,300	63·1	0	2·00	3·5
	926		32,500	64·4	0	2·00	3·5
Fe^{2+} (933 ml.)...	1024	15 *	3719	131·7	0·6	2·00	6·4
	963	14 *	3719	126·4	0·6	2·00	6·5
	965	14 *	3725	125·8	0·6	2·00	6·5
Co^{2+} (932 ml.)...	984		3730	182·5	0·7	2·00	9·2
	985		3721	181·9	0·7	2·00	9·2
	994		3726	183·7	0·7	2·00	9·2
	983		987	83·2	1·1	1·00	8·4
	962		969	81·7	1·1	1·01	8·4
	989		990	83·1	1·1	1·00	8·3
Ni^{2+} (933 ml.)...	986		3732	250·1	0·7	2·00	12·6
	992		3733	247·3	0·7	2·00	12·6
	992		3725	253·1	0·7	2·00	12·7
	995		997	121·3	1·1	1·00	12·1
	987		987	119·3	1·1	1·00	12·0
	966		966	114·4	1·1	1·00	11·8
Cu^{2+} (933 ml.)...	981	6103	6030	258·4	1·4	2·00	13·1
	978	6104	6021	258·1	1·5	2·00	13·0
	967	6106	6005	255·3	2·0	2·00	13·1
	971	508	1223	175·4	−0·3	1·00	18·0
	976	516	1232	175·9	−0·2	1·00	18·0
	969	510	1217	173·5	0·2	1·00	17·9
Zn^{2+} (941 ml.)...	972		3742	126·6	0·7	2·00	8·3
	985		3719	164·5	0·7	2·00	8·3
	987		3726	164·7	0·7	2·00	8·3
	986		989	68·8	1·1	1·00	6·9
	983		984	67·3	1·1	1·00	6·7
	963		963	64·2	1·1	1·00	6·6

* In the ferrous sulphate solution.

TABLE 2. *Thermodynamic and spectrophotometric data for the equilibria between diethylenetriamine and some metal*(II) *ions in* 0·1M-*potassium chloride at* 25°.

	Mn^{2+}	Fe^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
$-\Delta H_1$ [a] (kcal. mole^{-1})			8·15	11·85	18·00	6·45
$-\Delta H_2$,, ...			10·25	13·45	8·15	10·15
$-\Delta H_{1-2}$ [a] ,, ...	6·95	12·95	18·40	25·30	26·15	16·60
$-\Delta G_1$ [b] (kcal. mole^{-1})			10·90	14·45	21·55	12·00
$-\Delta G_2$ [b] ,, ...			8·00	10·90	7·10	7·50
$-\Delta G_{1-2}$ [b] ,, ...			18·90	25·35	28·65	19·50
ΔS_1 (cal. deg.$^{-1}$ mole^{-1})			9·0	8·5	12·0	18·5
ΔS_2 ,, ...			−7·5	−8·5	−3·5	−9·0
ΔS_{1-2} ,, ...			1·5	0·0	8·5	9·5
Dq $[M(H_2O)_6]^{2+}$ (cm.$^{-1}$)		1040 [c]	900 [d]	850 [c]		
Dq $[M\ den_2]^{2+}$ (cm.$^{-1}$)		1140	1100	1160		
$-\Delta H_{cryst.}$ (kcal. mole^{-1})	0	1·15	4·55	10·60		0
$-\Delta H_{1-2\ corr.}$,, ...	6·95	11·80	13·85	14·70		16·60

[a] Jonassen's thermodynamic values (ref. 3) for. $-\Delta H_1$, $-\Delta H_{1-2}$, in kcal. mole^{-1}, are, respectively: Mn 4, 9; Fe 9, 17; Co 9, 19; Ni 12, 25; Cu 20, —; Zn 8, —. McIntyre's values (ref. 4) are, respectively: Cu 18·9, 25·2; Zn 6·4, —. [b] Calculated from data for 20° and μ = 0·1M-potassium chloride (ref. 2) by using the enthalpy values obtained in the present work. [c] Cf. ref. 7. [d] Ballhausen and Jörgensen, *Acta Chem. Scand.*, 1955, **9**, 397.

successive steps of the reaction. Values of ΔG and ΔS could not be calculated for manganese and iron, as values of the formation constants in 0·1M-potassium chloride are not available. Nevertheless, in these two cases as well, the values of the ΔH_{1-2} could be determined. For this purpose a sufficient excess of base was used to allow complete formation of the $[M\ den_2]^{2+}$ ions. To make a rough estimate of the desired amount of this excess, the constants β_2 in (M-potassium chloride + potassium nitrate) by Jonassen *et al.*[3] were used. On the other hand, with manganese, which has the lowest constant of all, measurements made with different base : metal ratios from 307 to 357, gave the same value of ΔH_{1-2}. Table 2 also shows the

values of Dq for the ions $[M(H_2O)_6]^{2+}$ and $[M\,den_2]^{2+}$, which are needed for calculating $\Delta H_{1-2\ cryst.}$.

Discussion

The spectra of the $[M\,den_2]^{2+}$ complex ions [M = Fe(II), Co(II), Ni(II); den = diethylenetriamine] are found to resemble closely those of the corresponding hexa-coordinate complexes $[M\,en_3]^{2+}$ and $[M(NH_3)_6]^{2+}$. This shows that, for the diethylenetriamine complexes, too, the symmetry of the ligand field is essentially octahedral. In particular, the wavelengths of the " first " absorption band coincide, within experimental error, with those of the corresponding band of the complexes with three molecules of ethylenediamine.[7] The crystal-field stabilisation energy calculated from the spectroscopic values of Dq is therefore the same for complexes of types $[M\,den_2]^{2+}$ and $[M\,en_3]^{2+}$.

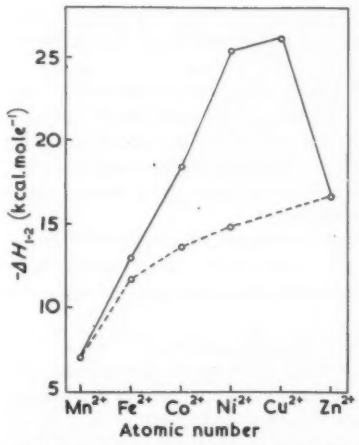
In the Figure the heats of formation ΔH_{1-2} are plotted against the atomic number: the upper curve refers to the experimental values; the lower one was obtained by applying the correction $\Delta H_{1-2\ cryst.}$ for the crystal-field stabilisation energy

$$\Delta H_{1-2\ cryst.} = (4n_e - 6n_\gamma)(Dq_{6H_2O} - Dq_{2den}).$$

For copper the crystal-field stabilisation energy was not calculated because of the pronounced tetragonal distortion due to the Jahn–Teller effect and also, as will be shown below, because it is doubtful how many copper–nitrogen bonds exist in the complex $[Cu\,den_2]^{2+}$.

The trend of the two curves is about the same as that of the corresponding curves for the heats of formation ΔH_{1-3} of the ethylenediamine complexes.[1] In particular the points representing the corrected heats for iron, cobalt, and nickel lie above the line joining manganese to zinc. This provides further evidence that the proposed linear interpolation between manganese and zinc [8] cannot be considered correct in every case.

The overall heats of formation of the diethylenetriamine complexes are all about 3—4 kcal. lower than the heats of the corresponding trisethylenediamine complexes. This could be due either to strain within the chelate rings or to the fact that the bonds between the metal and the secondary nitrogen atoms of the amines are weaker than those between the metal and the primary nitrogen atoms. The latter hypothesis is supported by the fact that the heats of formation for the compounds of alkylamines with different acceptors such as trimethylboron,[9] (diacetyl bisbenzoylhydrazono)nickel(II),[10] and the hydrogen ion,[11] show that dialkylamines are more weakly bound than monoalkylamines.



Experimental (——) *and corrected crystal-field stabilisation energy* (– – – –) *heats of formation of* $[M\,den_2]^{2+}$ *ions.*

Table 2 shows that, except for copper, the heat changes for the second step, ΔH_2, are larger than those for the first step, ΔH_1. The tendency of the successive heat changes to increase has already been noted among metal complexes with ethylenediamine. In the complexes with diethylenetriamine this increase is even more marked, particularly with zinc.

In the copper–diethylenetriamine system, the heat of reaction of the first ligand molecule is $-18{\cdot}00$ kcal. mole^{-1}, while that of the second molecule is only $-8{\cdot}15$ kcal. mole^{-1}.

[7] Jörgensen, Reports 10th Solvay Conf., Brussels, 1956.
[8] Orgel, Reports 10th Solvay Conf., Brussels, 1956.
[9] Brown, McDaniel, and Häfliger, in Braude and Nachod's " Determination of Organic Structures by Physical Methods," Academic Press Inc., New York, 1955, p. 642.
[10] Sacconi, Lombardo, and Ciofalo, *J. Amer. Chem. Soc.*, 1960, **82**, 4182; Sacconi and Lombardo, *ibid.*, 6266.
[11] Everett and Wynne-Jones, *Trans. Faraday Soc.*, 1939, **35**, 1380.

The value of the copper–nitrogen bond energy, taken as equal to half the heat of formation of the complex $[Cu\ en]^{2+}$, determined by various authors,[4,12] is about −6·5 kcal. mole^{-1}. Copper, therefore, behaves normally on the addition of the first molecule of diethylenetriamine, since the value of the heat of reaction ΔH_1, −18·00 kcal. mole^{-1}, is roughly equal to the heat of formation of three copper–nitrogen bonds, *viz.* −19·5 kcal. mole^{-1}. The difference of 1·5 kcal. mole^{-1} is, in effect, exactly half of what we found to be the difference between a trisethylenediamine complex and the corresponding bis-diethylenetriamine complex. McIntyre *et al.*,[4] on the other hand, found a value of −6·3 kcal. mole^{-1} for the heat of binding of a second diethylenetriamine molecule and concluded that only a fourth metal–nitrogen bond had been formed. On the contrary, we regard our calorimetric ΔH_2 value of −8·15 kcal. mole^{-1} as more reliable and therefore believe that it indicates the formation of more than one bond between copper and the second molecule of ligand. The fact that this value is less than expected for the formation of two copper–nitrogen bonds is probably due to the crystal-field stabilisation energy which is less for the complex $[Cu\ den_2]^{2+}$ than for $[Cu\ den]^{2+}$. In fact, the three nitrogen atoms in the latter ion very probably lie in one plane,[13] the remaining three co-ordination positions being occupied by three water molecules. If this is so, the resulting octahedral configuration will be tetragonally distorted and the ground state of the complex stabilised by a gain in the energy due to the removal of the degeneracy of the d_ε and d_γ orbitals caused by the tetragonal component of the electric field acting on the copper ion. In the complex $[Cu\ den_2]^{2+}$, on the contrary, this tetragonal distortion is considerably smaller. This is shown by the spectra in which, contrary to the rule of average environment, the absorption maximum of the "first" band of the $[Cu\ den_2]^{2+}$ ion is shifted towards the lowest frequencies (penta-amino-effect), as compared to that of $[Cu\ den]^{2+}$.[5] Consequently the crystal-field stabilisation energy decreases, so causing a lower heat of formation of the ion $[Cu\ den_2]^{2+}$. It should be remembered in this connection that the tetra-amino-configuration is already excluded by Jörgensen's study of the spectra of $[Cu\ den]^{2+}$ and $[Cu\ den_2]^{2+}$, which made him postulate [5] a penta- or hexa-co-ordination of the complex ion $[Cu\ den_2]^{2+}$.

The heat of formation of the complex $[Zn\ den]^{2+}$ is particularly low, even lower than the heat of formation of the $[Zn\ en]^{2+}$ ion [1] in which only two metal–nitrogen bonds are present. In this case, as well as for the $[Zn\ en_2]^{2+}$ ion,[1] we are forced to admit that the low heat change is due to the additional endothermic effect arising from the displacement of more than three water molecules from the first co-ordination sphere. As a consequence a tetrahedral ion of the type $[Zn(H_2O)\ den]^{2+}$ could be formed.[14]

The heat of formation of the complex $[Zn\ den_2]^{2+}$ is −16·60 kcal. mole^{-1}. Taking half the heat of formation of the $[Zn\ en]^{2+}$ complex,[1] *i.e.*, −3·5 kcal., as the strength of the zinc–nitrogen bond, one may conclude that at least five zinc–nitrogen bonds exist in the $[Zn\ den_2]^{2+}$ complex.

The entropy changes ΔS_1 and ΔS_{1-2} are all positive; the ΔS_1 values for cobalt and nickel are equal within experimental error. The higher value for copper agrees with the above-mentioned hypothesis [13] that the first molecule of diethylenetriamine is not bound on an octahedral face, as is probably the case with cobalt and nickel,[15] but is instead so disposed that the three bonds are co-planar. With copper, this planar configuration, though strained, is doubtless preferred because of the increased crystal-field stabilisation energy so obtained. The dipole moment of the non-planar configuration is roughly $\sqrt{3}$ times greater than that of the planar one. The $[Cu\ den]^{2+}$ ion will therefore be able to

[12] Poulsen and Bjerrum, *Acta Chem. Scand.*, 1955, **9**, 1407.
[13] Courtney, Gustafson, Chaberek, jun., and Martell, *J. Amer. Chem. Soc.*, 1959, **81**, 519.
[14] Martell and Calvin, "Chemistry of the Metal Chelate Compounds," Prentice-Hall, Inc., New York, 1953, p. 146.
[15] Barclay, *Rev. Pure Appl. Chem.*, 1954, **4**, 77.

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orientate fewer water molecules than the corresponding ions $[Ni\ den]^{2+}$ and $[Co\ den]^{2+}$, and the entropy of the final state will thus be higher.[16]

The value of ΔS_1 for zinc is even higher than that for copper. This seems to indicate that the introduction of a molecule of diethylenetriamine in the first co-ordination sphere of a zinc aquo-ion detaches more water molecules than it does from other aquo-cations, with a consequent increase in translational entropy.[17] This corroborates the above hypothesis of the formation of a tetrahedral $[Zn\ den]^{2+}$ ion.

The values of ΔS_{1-2} (which are all positive) can be divided into two groups: the first includes cobalt and nickel (1·5 and 0·0 cal. deg.$^{-1}$ mole^{-1}, respectively), and the second includes copper and zinc (8·5 and 9·5 cal. deg.$^{-1}$ mole^{-1}). For the last two ions the higher value of the overall entropy change can be explained by assuming that the complexes formed are less rigid than the corresponding complexes of the first group. This could agree with the hypothesis put forward by Jonassen *et al.*[3] that in the $[Cu\ den_2]^{2+}$ and $[Zn\ den_2]^{2+}$ ions the number of the co-ordinated nitrogen atoms is less than six. In this case, freedom of movement of the non-co-ordinated portions of the ligand molecules would contribute to the increase of the entropy. If the number of the co-ordinated nitrogen atoms were really less than six, the value of ΔH_{1-2} for the ion $[Zn\ den_2]^{2+}$ could not constitute a reference point in the Figure.

The changes of free energy during the formation of bisdiethylenetriamine complexes that have been reported in the literature [18] are roughly equal to those of the corresponding trisethylenediamine complexes. Nevertheless, as shown by the measured heats of formation, the nitrogen–metal bonds are stronger in the ethylenediamine complexes than in those of diethylenetriamine. The latter are, however, stabilised by the positive entropy term, whereas in the ethylenediamine complexes the entropy change is negative and varies from −13·0 to −8·5 cal. deg.$^{-1}$ mole^{-1}.

The entropy of formation of the hexamminometal(II) ions is known only for the nickel complex $[Ni(NH_3)_6]^{2+}$. For nickel, then, it is possible to compare the entropy changes for the hexa-co-ordinated complexes with ammonia, ethylenediamine, and diethylenetriamine severally, which contain an increasing number of chelate rings. The overall ΔS values are: $[Ni(NH_3)_6]^{2+}$, ΔS_{1-6} −42; [19] $[Ni\ en_3]^{2+}$, ΔS_{1-3} −11; $[Ni\ den_2]^{2+}$, $\Delta S_{1-2} = 0$ cal. deg.$^{-1}$ mole^{-1}. This marked increase in the entropy change, which stabilises the complexes having a greater number of chelate rings, must be ascribed, at least in part, to the increase in the number of free particles which takes place on complex formation, with a consequent increase in translational entropy.

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Institute of General Chemistry, The University of Palermo,
Palermo, Italy.
[Present address: Istituto di Chimica Generale dell' Università di Firenze,
Via Gino Capponi 9, Florence.] [*Received, January 25th*, 1961.]

[16] Chatt and Wilkins, *J.*, 1952, 4300; 1956, 525.
[17] Calvin and Bailes, *J. Amer. Chem. Soc.*, 1946, **68**, 949.
[18] Bjerrum, Schwarzenbach, and Sillén, "Stability Constants," Part I, *Chem. Soc. Special Publ. No.* 6, 1957.
[19] Yatsimirskii and Milyukov, *Zhur. fiz. Khim.*, 1957, **31**, 842.

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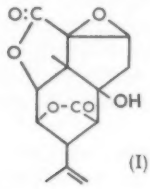
575. *Picrotoxin and Tutin. Part XI.*[1]

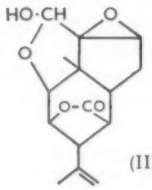
By G. F. Browne, R. B. Johns, and K. R. Markham.

The functional groups of tutin are defined as two five-membered lactones and two hydroxyl groups.

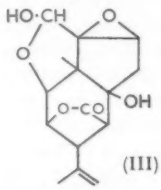
The poisonous constituent of the New Zealand species of *Coriaria*, known collectively [2] as "Tutu," was first isolated by Easterfield and Aston [3] and named tutin. Together with picrotoxinin,[2] $C_{15}H_{16}O_6$, coriamyrtin,[4] $C_{15}H_{18}O_5$, and mellitoxin,[5] $C_{15}H_{18}O_7$, tutin, $C_{15}H_{18}O_6$, forms a series of similar molecular formulæ and physiological properties. Of these bitters, picrotoxinin has been the most intensively studied, efforts culminating in structure (I) being suggested by Conroy.[6] From degradative experiments and Conroy's structure for picrotoxinin, Kariyone and Okuda [7] suggested structure (II) for coriamyrtin. The Japanese workers isolated from *Coriaria japonica* coriamyrtin and a second bitter principle coriarine,[8] which was later shown to be identical with tutin,[9] and because of the similarity of infrared spectra of tutin and picrotoxinin, and the common source of tutin and coriamyrtin, they suggested structure (III) for tutin,[7] *i.e.*, hydroxycoriamyrtin. Structure (III) fails in several respects: a hemiacetal is sufficiently acidic to be methylated with



(I)



(II)



(III)

diazomethane, and such a reaction has been observed in the picrotoxinin series [10] in which the lactones are placed similarly to that shown in (III); tutin, however, is recovered from attempted methylation with diazomethane; structure (III) implies that oxidation of tutin would give picrotoxinin but in practice a ketone [11] is formed; picrotoxinin, when heated with alkali, undergoes characteristic degradation; [12] and after slow hydrolysis of the hemiacetal, similar degradation of tutin may be expected since all prerequisites for degradation are present in the molecule; [1] tutin, however, displayed an unsuspected stability to boiling dilute alkali and reacted in a manner most easily explained as the conversion of a dilactone into a dicarboxylic acid. Lastly, a closer examination of the infrared spectra of various tutin derivatives revealed further inconsistencies with the monolactone formulation (III). A re-assessment of the chemistry of tutin was indicated and the results are reported here.

Earlier work has shown tutin to be a polyol, but the number and nature of the hydroxyl groups were not clear from the conflicting reports.[8,9,13] Four different acetates of tutin have been reported and Okuda's [9] attempt to reconcile melting points ranging as widely as

[1] Part X, *J.*, 1960, 1965.
[2] Barth and Kretschy, *Monatsh.*, 1884, **5**, 65.
[3] Easterfield and Aston, *J.*, 1901, **79**, 120.
[4] Riban, *Compt. rend.*, 1866, **67**, 476, 680.
[5] Sutherland and Palmer-Jones, *N.Z. J. Sci. Technol.*, 1947, **29**, *A*, 114.
[6] Conroy, *J. Amer. Chem. Soc.*, 1957, **79**, 1726.
[7] Kariyone and Okuda, *J. Pharm. Soc. Japan*, 1953, **73**, 928.
[8] Kinoshita, *J. Chem. Soc. Japan*, 1930, **51**, 99.
[9] Okuda, *Pharm. Bull. Japan*, 1954, **2**, No. 3, 185.
[10] Johns, Slater, Woods, Brasch, and Gee, *J.*, 1956, 4715.
[11] Fletcher, Hall, Richards, Slater, and Watson, *J.*, 1954, 1953.
[12] Sutter and Schlittler, *Helv. Chim. Acta*, 1947, **30**, 403, 2102; 1949, **32**, 1855, 1860.
[13] Slater, *J.*, 1943, 50.

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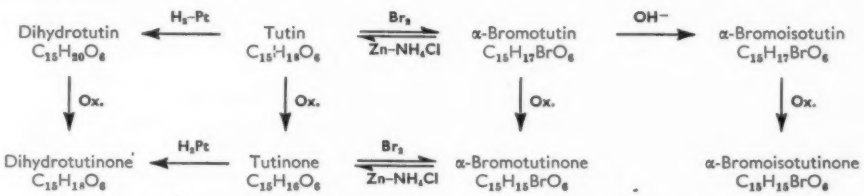
177° to 240° was unconvincing, particularly when elementary analyses and acetyl determinations were neglected. A re-investigation has shown that tutin is readily acetylated with acetic anhydride and pyridine at water-bath temperature giving a single monoacetate, m. p. 183°. When tutin was refluxed for 1·5 hr. in acetic anhydride with sodium acetate as catalyst, a diacetate, m. p. 203°, was obtained, which presumably corresponds to Okuda's [9] of similar melting point. If tutin monoacetate was further acetylated with sodium acetate as catalyst, a third acetyl derivative, also a diacetate, m. p. 185°, was isolated as the only product. From the published data, it is not possible to determine whether the mono- or di-acetate corresponds with Slater's acetyltutin,[13] m. p. 177°, or Kinoshita's [8] and Okuda's [9] acetate, m. p. 183°. In Part VII [11] it was suggested that tutin possessed at least two hydroxyl groups, and on the basis of a monolactone hypothesis and a Zerewitinoff determination of four active hydrogen atoms, that tutin was possibly a tetrahydroxy-compound. Tutin monoacetate showed hydroxyl absorption in the infrared spectrum which was absent from both the diacetates. The formation of these compounds being assumed to be simple acetylation of the hydroxyl groups, tutin itself is then a dihydroxy-compound.

Further support comes from consideration of the oxidation products. Dihydrotutin, α-bromotutin, and α-bromoisotutin have been oxidised, though in poor yield, to the corresponding ketones by chromic oxide in acetic acid.[11] By oxidation with chromic acid in acetone,[14] nearly quantitative yields of ketones were obtained. In particular, tutin is readily oxidised to tutinone and the double bond (1645 cm.$^{-1}$) is unaffected. (The suffix -one conveniently distinguishes the ketone from the corresponding hydroxy-compound and this nomenclature is adopted in this paper. Thus dehydrotutin [11] becomes tutinone.) Similarly, α-bromotutinone could be readily obtained in high yield from α-bromotutin. The inter-relationships between the hydroxy-compounds and ketones are shown in the scheme below.



The fact that tutinone can be obtained by oxidation of tutin under both acid and basic (chromic oxide in pyridine) conditions, together with the consistency of elemental analytical data between the series of compounds shown above, suggests that the formation of tutinone is the simple oxidation of a secondary alcohol. There is no fact in the known chemistry of these ketones which is inconsistent with this view. The remaining hydroxyl group is probably tertiary, indicated by the relative difficulty of further acetylation of monoacetyltutin; stability of tutinone to oxidation by chromic acid; and most significantly, the nature of the bromination reaction of tutin.

Both tutinone and dihydrotutinone show hydroxyl absorption in the infrared spectrum which in the case of tutinone is removed by bromination to form α-bromotutinone, which is saturated. Similarly, α-bromotutin shows hydroxyl absorption which is absent from its monoacetate. These facts are consistent with the view that tutin is a dihydroxy-compound, and that bromination involves both the double bond and the hydroxy-group, forming a monobrominated derivative. This reaction is parallel to the formation from picrotoxinin (I) of α-bromopicrotoxinin for which structure (IV) has recently been confirmed by crystallographic methods.[15]

[14] Jones, Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2555.
[15] Craven, *Tetrahedron Letters*, 1960, No. 19, 21.

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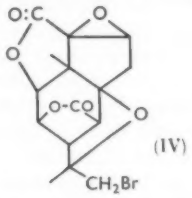
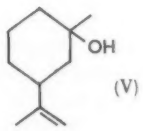
A terminal methylene group in tutin was established by the formation of formaldehyde on ozonolysis [11] but the C_{14} fragment was not isolated. When this reaction was repeated, formaldehyde was again identified and the residue gave a positive



(IV)



(V)

test for a methyl ketone, strongly suggesting the presence of an isopropenyl side chain, hitherto assumed,[7] and which was later confirmed by nuclear magnetic resonance data (see Part XII). It seems reasonable to assume that in tutin a 1,3 relation exists between a suitably reactive hydroxyl group and the isopropenyl side chain as in picrotoxinin. For the reasons outlined above the second hydroxyl group is probably tertiary and is positioned as in the partial formulation (V).

On the basis of the infrared absorption in the carbonyl region of a limited number of derivatives, tutin was considered to be a monolactone.[11] This view was accepted and in turn supported by the Japanese group with their interpretation of the infrared absorption spectra of tutin and α-bromotutin.[16] The resolution of the carbonyl maximum in the spectrum of picrotoxinin is not very pronounced and the resolution has been comparable in our experience in the case of tutin. In particular, for tutin, the lactone absorption maximum, especially for the spectrum in solution, is unsymmetrical with a marked shoulder at higher wave-numbers. With the corresponding ketones, both in solution and as solid, resolution of the lactone absorption band has been marked. The Table lists the maxima in the functional regions, and it should be noted that the lactone-carbonyl

Light-absorption maxima.

	Ultra-violet (mμ)	Infrared (cm.$^{-1}$) Hydroxyl	Lactone	Ketone	Olefin
Picrotoxinin (Nujol)		3464	1790—1766br		1649
Tutin (Nujol)		3510, 3450	1779—1759br		1647
,, ($CHBr_3$)			1789sh, 1776		
Dihydrotutin (Nujol)		3460, 3390	1784, 1756		
,, ($CHBr_3$)			1780, 1771		
Dihydrotutinone (Nujol)		3412	1810—1790br	1705	
,, ($CHBr_3$)			1799sh, 1784		
Tutinone (Nujol)	305	3410	1806, 1794	1705	1645
,, ($CHBr_3$)			1792, 1775	1715	
Ozonolysis product (KBr)	276	3512, 3430	1785, 1769	1695	
α-Bromotutin ($CHBr_3$)			1770		
α-Bromotutinone ($CHBr_3$)	309		1800, 1775	1717	
α-Bromoisotutin (KCl)			1760, 1751br		
α-Bromoisotutinone (Nujol)	314		1780, 1756	1739	

br = broad; sh = shoulder.

absorption maxima of the ketones display marked resolution, consistent with the presence in tutin of a dilactone. The formation of the ketones involved an oxidation step and it may well be argued that acidic conditions have involved simultaneous oxide rupture and oxidation, or other rearrangement in their formation. We rejected this hypothesis on other grounds discussed above, and the spectra of non-oxidised derivatives, *e.g.* dihydrotutin itself, which is resolved in both solution and the solid, as was the ozonolysis product, support this contention. It was also possible to resolve the carbonyl maximum in the infrared spectrum of α-bromoisotutin which is formed by alkaline isomerisation of

[16] Kariyone and Okuda, *Bull. Inst. Chem. Res. Kyoto Univ.*, 1953, **31**, No. 5.

α-bromotutin. The spectroscopic evidence is therefore in complete accord with a dilactone hypothesis.

Support for the monolactone view is found in the results of quantitative titrations of tutin and dihydrotutin,[5,17] which were reported as potentially monobasic under conditions in which picrotoxinin and dihydropicrotoxinin were found to be potentially dibasic. Re-examination of the conductimeric titration curve revealed a reproducible initial uptake of about 1·4 equivalents of cold alkali for tutin, tutinone, and α-bromoisotutin; a titre in excess of experimental error for one equivalent, but which would be consistent with the slow hydrolysis of a second lactone. When the rate of hydrolysis of tutin with 0·1N-sodium hydroxide at 45° was followed, a maximum uptake of 2 equivalents was reached after 11 hours. The same maximum titre was obtained from tutin, tutinone, and α-bromoisotutin by heating them for 15 min. with dilute alkali. These results are consistent with a dilactone structure but it must be noted, in the case of tutin and tutinone, that the reaction is irreversible with either hot or cold alkali, *i.e.* unlike dihydropicrotoxinin or α-bromoisotutin with cold alkali, the tutin derivatives could not be recovered. We had earlier observed that unlike picrotoxinin, tutin could be boiled with alkali, particularly if the solid was first dissolved in the cold alkali, without the development of the degradation colour so characteristic of many picrotoxinin compounds. (If tutin was not previously dissolved, a transient yellow colour could be observed in the solution immediately above the crystals.) If tutin possessed structure (III), degradation should occur.[1] Paper-chromatographic analysis of the alkaline solutions showed the presence of one acidic component only, and both its R_F value and reaction with the developing spray suggested a dibasic nature. Physical methods, then, left little doubt of the potentially dibasic nature of tutin.

Conventional methods which might have yielded carboxylic acid derivatives from tutin by analogy with picrotoxinin, but which in fact resulted in transformations into saturated isomers were summarised in Part VII.[11] Dihydrotutin with hot sodium carbonate has been reported to yield [18] an acid, $C_{15}H_{24}O_8$, and with cold sodium methoxide in methanol an ester,[19] $C_{16}H_{24}O_8$. Little more was known, however of the chemistry of these compounds.

Hydrolysis of tutin with cold dilute aqueous alkali gave no significant yield of crystalline material. Hot dilute aqueous alkali transformed tutin in high yield into a hydrated acid, tutindicarboxylic acid. No evidence has been obtained of the presence in the reaction mixture of any other transformation product. It is formulated as a dicarboxylic acid on the following evidence: Analysis indicates $C_{15}H_{22}O_8$, and the infrared shows absorption in the carbonyl region at 1715—1700 cm.$^{-1}$ only; the double bond is retained; it titrates as a dibasic acid, forms a diphenacyl derivative, and gives a crystalline monomethyl ester with diazomethane, which shows maxima at 1725 (CO_2Me) and 1703 cm.$^{-1}$ (CO_2H).

Methanolysis of picrotoxinin yields dimethyl picrotoxinindicarboxylate and methyl picrotoxate. The ratio of the yields varies according to the concentration of sodium methoxide.[20] With tutin, catalytic quantities of sodium methoxide did not bring about reaction [21] but with one equivalent a good yield of a crystalline ester, $C_{16}H_{24}O_8$, was obtained. This ester contains one carboxyl group (1746, CO_2Me; 1722 cm.$^{-1}$, CO_2H), shows 1·3 acidic centres in titration against cold alkali, and, two after hydrolysis with hot alkali, rapidly decolorises ethereal diazomethane solution, and is unsaturated. It readily forms a triacetate, $C_{22}H_{30}O_{11}$, which still shows hydroxyl absorption in the infrared spectrum. For these reasons we assign it the structure of a monomethyl ester of a dicarboxylic acid rather than that of a monoester monolactone. The mother liquors from the methanolysis yielded an intractable gum which was not further investigated.

[17] Benstead, Brewerton, Fletcher, Martin-Smith, Slater, and Wilson, *J.*, 1952, 1042.
[18] Wilson, M.Sc. Thesis, Victoria Univ. of Wellington, 1950.
[19] Watson, M.Sc. Thesis, Victoria Univ. of Wellington, 1952.
[20] Benstead, Gee, Johns, Martin-Smith, and Slater, *J.*, 1952, 2292.
[21] Fletcher, M.Sc. Thesis, Victoria Univ. of Wellington, 1951.

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The dilactone nature of tutin is demonstrated beyond reasonable doubt. It is possible now to assign functions to all six oxygen atoms in tutin as two γ-lactones, and one secondary and one tertiary hydroxyl group. In consequence, the formulation (III) suggested by the Japanese workers for tutin is untenable.

Experimental

Acetylation of Tutin.—(*a*) Tutin (0·5 g.), acetic anhydride (10 ml.), and pyridine (1 ml.) were heated on a steam-bath for 3 hr., then kept overnight at room temperature. After removal of solvent under reduced pressure, the residue was recrystallised from aqueous methanol to give *monoacetyltutin*, m. p. 183° (Found: C, 60·8; H, 5·9; Ac, 13·8. $C_{17}H_{20}O_7$ requires C, 60·7; H, 5·9; 1Ac, 12·8%); $\nu_{max.}$ (potassium bromide disc) 3547m, 3432m, 1781s, 1741s, and 1643w cm.$^{-1}$.

(*b*) Tutin (0·2 g.), sodium acetate (0·05 g.), and acetic anhydride (10 ml.) were heated for 1·5 hr. at 140°. After removal of solvent, the residual oil was washed with water, dissolved in aqueous methanol, and treated with charcoal. The filtrate yielded crystals, which after recrystallisation from aqueous methanol, gave a *diacetyltutin*, m. p. 204° (Found: C, 60·3; H, 5·7; Ac, 22·2. $C_{19}H_{22}O_8$ requires C, 60·3; H, 5·9; 2Ac, 22·2%); $\nu_{max.}$ (in Nujol) 1795s, 1750s, 1732s, and 1650w cm.$^{-1}$.

(*c*) Monoacetyltutin (0·2 g.), sodium acetate (0·05 g.), and acetic anhydride (10 ml.) were refluxed for 1 hr. The solution was worked up as in (*b*) to give a *diacetate*, which crystallised in needles from aqueous methanol, and had m. p. 185° (mixed m. p. with monoacetate was much lower) (Found, in sample sublimed at 156°/0·1 mm.: C, 60·6; H, 5·7; Ac, 22·6%, as required for $C_{19}H_{22}O_8$).

Oxidation of Tutin and Derivatives.—(*a*) Tutin (0·5 g.) was dissolved in acetone (10 ml.) and a solution of chromic acid [14] was added, dropwise, until the mixture remained yellow. The solvent was removed under reduced pressure, the residue was washed with water, and the precipitate was recrystallised from ethanol, yielding tutinone (0·4 g.), m. p. 243° (decomp.); $\lambda_{max.}$ (in ethanol) 305 mμ (log ε 1·22).

In a similar manner the following were oxidised in high yields: dihydrotutin yielded dihydrotutinone, m. p. 245° (decomp.). α-Bromotutin gave α-bromotutinone, m. p. 171°, $\lambda_{max.}$ (in ethanol) 309 mμ (log ε 1·13). α-Bromoisotutin gave α-bromoisotutinone, m. p. 273°.

(*b*) A solution of tutin (0·5 g.) in pyridine (10 ml.) was added to a slurry of chromic oxide (2 g.) and pyridine (20 ml.), and the mixture kept overnight at room temperature. Pyridine was removed in a vacuum and water was added to the residue. Carbon dioxide was bubbled through the mixture, and the buff-coloured precipitate was collected (0·25 g.), recrystallised from ethanol, and treated with charcoal; it yielded tutinone, m. p. and mixed m. p. with an authentic sample, 245°.

Bromination of Tutinone.—A solution of tutinone (0·1 g.) in hot aqueous (15 ml.) dioxan (5 ml.) was treated with bromine. The volume was reduced to *ca.* 10 ml. and on cooling, α-bromotutinone (0·1 g.) crystallised. After recrystallisation from ethanol it had m. p. 165°, undepressed by an authentic sample.

Ozonolysis of Tutin.—Tutin (0·5 g.) was dissolved in acetic acid (25 ml.) and ethyl acetate (3 ml.), and the solution, cooled in an ice bath, was oxidised by a slow stream of ozone and oxygen for 2·5 hr. Water (5 ml.) and zinc dust (1 g.) were added, the suspension was heated on a water-bath for 15 min., excess of zinc filtered off, and the filtrate reduced to dryness in a vacuum. The distillate, when treated with 2,4-dinitrophenylhydrazine in 2N-sulphuric acid, yielded a heavy precipitate of formaldehyde 2,4-dinitrophenylhydrazone (m. p. and mixed m. p.). The solid residue was recrystallised from ethyl acetate–ethanol and yielded a slightly impure product, m. p. *ca.* 240°; $\lambda_{max.}$ (in ethanol) 276 mμ; $\nu_{max.}$ (potassium bromide disc) 3545, 3460, 1793s, 1773s, and 1697s cm.$^{-1}$. This material (0·05 g.) was oxidised with potassium iodide (10%; 10 drops) and sodium hypochlorite (20 drops), and the precipitate crystallised from ethanol; it had m. p. 115° undepressed by an authentic sample of iodoform, m. p. 116°.

Tutindicarboxylic Acid.—Tutin (1 g.) was dissolved in 0·1N-aqueous sodium hydroxide (70 ml.) and the solution refluxed for 15 min. The colourless solution was cooled, acidified to pH 2 with concentrated hydrochloric acid, and continuously extracted with ethyl acetate. To the first 24 hours' extract, a few drops of water were added and the whole reduced to a small volume, from which clusters of needles (40% yield) were obtained. Recrystallised from wet

ethyl acetate and dried to constant weight, the *tutindicarboxylic acid* had m. p. 198° (Found: C, 54·4; H, 6·7. $C_{15}H_{22}O_8$ requires C, 54·5; H, 6·7%); $\nu_{max.}$ (in Nujol; hydrated acid, m. p. 98°) 3385 br, 1715—1700, and 1640 cm.$^{-1}$. More (30%) acid was obtained when the aqueous reaction mixture was taken to dryness in a vacuum, excess of hydrochloric acid removed as azeotrope, and the residue crystallised from wet ethyl acetate.

The *monomethyl ester* was prepared by treatment with diazomethane until a yellow colour just persisted. Crystallisation from methanol and ether yielded needles, m. p. 205° (Found: C, 55·7; H, 6·7. $C_{16}H_{24}O_8$ requires C, 55·8; H, 7·0%); $\nu_{max.}$ (potassium bromide disc) 3524, 1725sh, 1703s, and 1640 cm.$^{-1}$. The *p*-bromophenacyl ester was prepared by refluxing for 3 hr. tutin (0·2 g.) in 0·1N-sodium hydroxide (8·6 ml.) and *p*-bromophenacyl bromide (0·5 g.) with sufficient ethanol to ensure solution. When cool, unchanged phenacyl bromide was filtered off and then the *di-p-bromophenacyl ester* was obtained; this was recrystallised from aqueous ethanol to constant m. p. 140° (Found: Br, 21·9. $C_{31}H_{32}Br_2O_{10}$ requires Br, 22·1%).

Tutin and Sodium Methoxide.—(The yields in this reaction varied; the following reaction conditions gave the best results.) A solution of sodium methoxide (2 mol.) in dry methanol was added, dropwise, to an ice-cold solution of tutin (1 g.) in dry methanol, and the mixture set aside overnight. Sufficient glacial acetic acid was added to acidify the solution, and the solvent was then removed in a vacuum. The residue was crystallised from aqueous methanol to give amorphous material (0·6 g.) which after further crystallisation gave a *monomethyl ester*, m. p. 220° (Found: C, 56·0; H, 6·6; OMe, 8·7. $C_{16}H_{22}O_8$ requires C, 56·1; H, 6·5; 1OMe, 9·1%); $\nu_{max.}$ (in Nujol) 3530s, 3450s, 3360s, 1746s, 1722s, and 1642w cm.$^{-1}$. The methyl ester was acetylated with acetic anhydride and pyridine giving a *triacetate*, m. p. 84° (with previous softening) (Found, in a sample sublimed at 190°/0·1 mm.: C, 55·9; H, 6·4; Ac, 25·4; active H, 0·48. $C_{22}H_{30}O_{11}$ requires C, 56·2; H, 6·4; 3Ac, 27·4; 2 active H, 0·42%). The methyl ester in water decolorised bromine water and a methanol solution decolorised diazomethane solution.

Conductimeric Titrations.—These were carried out in the usual way: a 20-ml. cell containing platinum electrodes comprised one arm of a Wheatstone bridge and the resistance of a solution, made from a known weight of compound in 0·1N-sodium hydroxide, was determined, as a back-titration was carried out. The potential acidity of the sample was calculated from a plot of conductance against quantity of standard acid.

(*a*) *Tutin.* (i) At room temperature—1·4. (ii) At 45°—after 11 hr. a maximum titre of 2 was attained. (iii) Refluxed for 15 min.—2.

(*b*) *Tutinone.* (i) At 0°—1·48. (ii) 85° for 15 min.—a titre of 2·0.

(*c*) *Tutindicarboxylic acid* (titrated after 35 min.)—2·0.

(*d*) *Tutin + sodium methoxide.* (i) Room temp.—1·35. (ii) After boiling—2·0.

(*e*) *α-Bromoisotutin.* The compound was dissolved in dioxan to ensure solution. (i) At room temp.—1·45 (unchanged material was recovered from this titration). (ii) After boiling—2·0.

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VICTORIA UNIVERSITY OF WELLINGTON,
WELLINGTON, NEW ZEALAND.
[Present address (R. B. J.): UNIVERSITY OF MELBOURNE,
PARKVILLE, N.2, VICTORIA, AUSTRALIA.]

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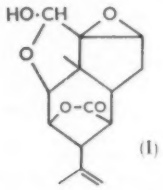
576. *Picrotoxin and Tutin. Part XII.*[1] *The Structure of Tutin.*

By R. B. Johns and K. R. Markham.

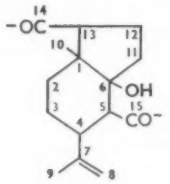
The structure of tutin is shown to be (III).

In Part XI [1] the functional groups of tutin, $C_{15}H_{18}O_6$, were defined as two γ-lactones and two hydroxyl groups, one secondary and the other tertiary, thereby accounting for all of the oxygen atoms in the molecular formula. Any attempt to position the functional groups, however, emphasised the assumed basis of tutin chemistry, *i.e.*, the lack of any experimental evidence relating the carbon skeleton to that of picrotoxinin.

Coriarine, later identified as tutin, was isolated from the same plant as coriamyrtin [2] and since this last compound was formulated as (I), it was reasonable to assume a picrotoxinin carbon skeleton for tutin. Nevertheless, during our investigations not one transformation product could be oxidised to a ketone to which a five-membered cyclic carbonyl function could unambiguously be assigned. The molecular formula for tutin requires a bicyclic ring system, and the choice of a decalin or an indane ring system could not be made from results of chemical degradations, which in our own experience had proved



(I)



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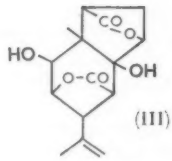

(III)

fruitless. A decision, however, was possible when it was appreciated that an indane system of the picrotoxinin type required the presence of an angular methyl group. Kuhn–Roth estimations were unhelpful, although consistent with similar determinations on picrotoxinin. The nuclear magnetic resonance spectrum of tutin * showed decisively the presence of an angular methyl group, and confirmed the presence of an isopropenyl side chain. The carbon skeleton, consequently, must be that of an indane system and it is reasonable to conclude, further, that the lactone carbonyl groups are placed similarly as in picrotoxinin. We shall develop our thesis on this basis and present evidence which justifies this assumption.

There is no free hydroxyl group alpha to a lactone carbonyl since tutin is not methylated by diazomethane; consequently the tertiary hydroxyl group, which is involved in the facile and stereospecific bromination reaction, can be placed confidently at position 6; this places the isopropenyl side chain at position 4. The similarity of the bromination in both the picrotoxinin and the tutin series enabled a partial formulation to be suggested in Part XI, and this can now be expanded to (II).† The secondary hydroxyl group must be placed in the six-membered ring since oxidation leads to tutinone,[1] a six-membered cyclic ketone (ν_{CO} 1705 cm.$^{-1}$). Tutin is not oxidised by periodic acid, consequently the two hydroxyl groups are not adjacent. From the carbon skeleton (II), the free hydroxyl group must be at position 2 or 3, and the precise position follows from the

* We are most grateful to Dr. N. Sheppard, of the University of Cambridge, for the determination of the spectra and his generous help in their interpretation.

† If coriamyrtin [1] is brominated to form a monobromo-derivative in which the double bond is saturated and the hydroxyl group has been removed, then this is sterically impossible for a compound with structure (I). It is probable that this formulation is incorrect for coriamyrtin, but the published chemistry is limited and it is not possible to suggest an alternative structure on a basis of anything better than speculation.

[1] Part XI, preceding paper.
[2] Kinoshita, *J. Chem. Soc. Japan*, 1930, **51**, 99.

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nature of the isotutin derivatives. α-Bromoisotutin is formed by alkaline isomerisation of α-bromotutin, and the view that this represents the isomerisation of a lactone [3] is supported by comparison of the infrared spectra of these compounds, particularly of the derived ketones.[1] The secondary hydroxyl group in α-bromoisotutin is unlikely to be identical with the hydroxyl in α-bromotutin, unless, in the isomerisation, a more profound rearrangement has occurred involving both lactones and leaving the original hydroxyl group unaffected. The isomerisation of monoacetyl-α-bromotutin [4] to α-bromoisotutin suggested that a new hydroxyl group arose in the transformation but was not conclusive. Stronger evidence came from the marked difference in ease of oxidation of α-bromotutin and α-bromoisotutin to the corresponding ketones. Whereas the former was readily oxidised at 37°, the latter required several hours for completion, comparable to the rate of oxidation of β-bromopicrotoxinic acid.[5] Light-absorption data emphasised the difference.[1] Ketones of the tutin series showed maxima about 1705 cm.$^{-1}$ and 3050 Å, which were raised in α-bromotutinone to 1717 cm.$^{-1}$ and 3090 Å. These values contrast with maxima for α-bromoisotutinone at 1739 cm.$^{-1}$ and 3140 Å, which were almost identical with those for oxo-β-bromopicrotoxinic acid [5] at 1740 cm.$^{-1}$ and 3140 Å. For these reasons we place the free hydroxyl group in α-bromoisotutin at position 3. In tutin, therefore, the secondary hydroxyl group is at position 2. There were other considerations, apart from a process of elimination, which also led to the same conclusion. Tutinone did not form a benzylidene derivative nor was it oxidised by selenium dioxide, which suggested that there were no methylene groups adjacent to the carbonyl. Significantly, bromination of tutinone is a reversible reaction, which would be expected if the carbonyl group were at position 2. With the free hydroxyl group in tutin at position 2, the potential hydroxyl at position 3 must be present as a lactone and since this is five-membered,[1] the lactone carbonyl will be at position 5; this agrees with the thesis that $C_{(15)}$ is placed as in picrotoxinin. Tutin, on this basis, should also possess a potential glycol unit.

Acid periodate did not react with tutin, but after alkaline hydrolysis, when two acidic centres were known to be present, sodium metaperiodate showed ready uptake of two equivalents with slower continuing oxidation, remarkably similar to periodate oxidation of hydrolysed picrotoxinic dilactone.[6,7] A 2,3-glycol in picrotoxinin derivatives did not normally show uptake greater than the expected one equivalent, which suggested a second potential glycol unit in tutin associated with structural features that permitted further oxidation. When α-bromotutin, after alkaline hydrolysis and with two acidic centres present,[1] was oxidised with sodium metaperiodate, only one equivalent of periodate reacted. The tertiary hydroxyl group is associated with the potential second glycol and, therefore, the remaining potential hydroxyl group is at position 11. This is in agreement with the placing of a carbonyl at position 13. It is possible at this stage to place all the oxygen atoms in tutin and thus derive structure (III). The free hydroxyl group at position 2 prohibits alternative closures of the lactone carbonyl groups.

The formation of α-bromoisotutin [3] is interpreted as the isomerisation of a γ-lactone to a δ-lactone. This is demonstrated most clearly in the infrared spectrum of the ketones, where the lactone maxima in α-bromotutinone at 1800 and 1775 cm.$^{-1}$ change in α-bromoisotutinone to 1780 and 1756 cm.$^{-1}$, and we suggest structure (IV) for α-bromoisotutinone. This formulation not only accounts for the remarkable similarity of light-absorption data to that for oxo-β-bromopicrotoxinic acid but predicts that debromination should take a course similar to that with the latter compound. When the debromination was carried out it was found that if the time of reaction was short, some α-bromoisotutinone was recovered, and from the mother liquors a dilactone, $C_{15}H_{16}O_6$, with infrared maxima at 1764, 1704, and 1618 cm.$^{-1}$, was obtained. From the near-identity of the relevant portion

[3] Fletcher, Hall, Richards, Slater, and Watson, *J.*, 1954, 1953.
[4] Johnson, Thesis, Victoria University of Wellington, New Zealand, 1955.
[5] Carman, Hassan, and Johns, *J.*, 1959, 130.
[6] Conroy, *J. Amer. Chem. Soc.*, 1957, **79**, 1726.
[7] Carman, Coombe, Johns, and Ward, *J.*, 1960, 1965.

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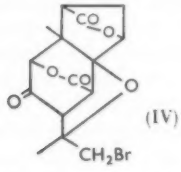
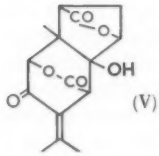
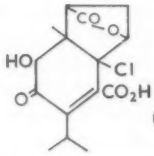
of the infrared spectrum with that shown by the acid, m. p. 219°, reported in Part IX,[5] *viz.* 1764, 1708, and 1615 cm.$^{-1}$, structure (V) is suggested for this compound. If the reaction time for the debromination was increased, the product obtained in good yield was a monochloro-acid, $C_{15}H_{17}ClO_6$, showing light-absorption maxima at 1742, 1727, 1685, and 1608 cm.$^{-1}$ and 2540 and 3200 Å [cf. the acid, m. p. 251°,[5] with maxima at 1675 and 1600 cm.$^{-1}$ (unsaturated ketone) and at 2470 and 3180 Å], and structure (VI) is



(IV)

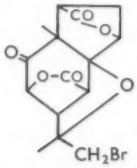


(V)

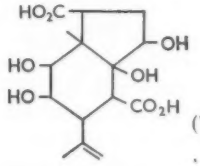


(VI)

suggested for this acid because it reacted with one equivalent of lead tetra-acetate. In working up the product, conditions similar to those for the Lucas test were employed, which accounts for the substitution by halogen. It also emphasises the lack of steric hindrance to reaction with the 6-hydroxyl group, which is a consequence of the presence of an endocyclic double bond. Of further interest is the fact that in the picrotoxinin series[5] the analogous reaction forms a lactone in which the 15-carbonyl group closes to position 12; in tutin where this is not possible, it appears as a carboxyl group.



(VII)



(VIII)

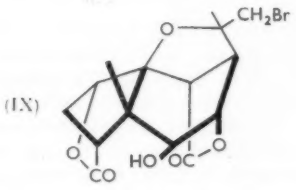
α-Bromotutinone may be represented as (VII). Under the same reaction conditions as were used to isomerise α-bromotutin, the ketone gave in high yield a product, $C_{15}H_{17}BrO_7$, for which lactone absorption only remained in the carbonyl region of the infrared spectrum. This reaction is interpreted as saturation of the carbonyl group with formation of a lactol, a reaction not unusual for δ-keto-acids,[8] and, in keeping with the reversibility or such reactions, with diazomethane the lactol gave a monomethyl ester monomethyl ether, $C_{17}H_{21}BrO_7$.

Tutin and tutindicarboxylic acid reacted readily with two equivalents of alkaline or acid periodate, respectively, with further uptake of reagent, and this at first appeared anomalous before structure (III) was finally derived. Further oxidation was due to subsequent attack at position 5 after initial cleavage (cf., acetoacetic acid and periodic acid[9]). When reaction with lead tetra-acetate was followed, α-bromotutin after alkaline hydrolysis reacted with one equivalent only, but tutindicarboxylic acid reacted rapidly with two equivalents with a marked drop in rate to a maximum of a third. This is in good agreement for structure (VIII) for tutindicarboxylic acid.

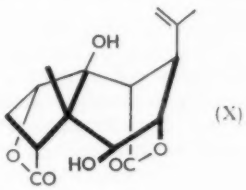
Neotutin[3] can be accounted for on the basis of structure (III) by the isomerisation of the isopropenyl side chain to an isopropylidene grouping. β-Tutin[3] is formed by addition across the double bond of the 6-hydroxyl group to give (IX; Br = H) in the same way as α-picrotoxinic acid isomerises to β-picrotoxinic acid,[3] and once the conformation is stabilised by the formation of an oxygen bridge, alkaline isomerisation of the 15-carbonyl to give a δ-lactone involving the 2-hydroxyl group, accounts for the formation of γ-tutin,[3] a member of the isotutin series.

[8] W. Hückel, "Theoretical Principles of Organic Chemistry," Elsevier, Amsterdam, 1955, Vol. I, p. 291.
[9] Manners, *R.I.C. Lectures, Monographs, and Reports*, 1959, No. 2.

The conformation of tutin follows from that for α-bromotutin, which in turn must be very similar to that suggested for α-bromopicrotoxinin.[10] The hydroxyl group at position 2 must be axial to permit isomerisation to the isotutin series. The cyclohexane ring is in a half-chair conformation to permit ready bromination. If the ring junction is *cis*, then the conformation of α-bromotutin will be (IX), and hence (X) will represent tutin. This



(IX)



(X)

conformation accounts for the non-lactonisation of the 14-carbonyl with the 6-hydroxyl and also with the 2-hydroxyl group, because in this latter case the two groups are not within easy bonding distance, and finally it explains the relative stability of one lactone to hydrolysis.

Experimental

Kuhn–Roth Estimations.—Picrotoxinin, 6·0; tutin, 5·3; dihydrotutinone, 7·4; tutinone, 7·9. 1*C*-Methyl requires 9·3; 9·2; 9·2; and 9·2%, respectively.

Nuclear Magnetic Resonance Determinations.—These were made at 40 Mc./sec. and with water as a standard: tutin (in D_2O), σ at 4·05; monoacetyltutin (in $CHCl_3$), σ at 4·05, 3·45 and +0·30; picrotoxinin (in dioxan), σ at 4·15 (angular methyl), 3·45 (CH_3–[C=CH_2]) and +0·40 (doublet; >C=CH_2).

Periodic Acid Oxidations.—(*a*) Tutin (0·0241 g.) was dissolved in 0·1N-sodium hydroxide (3 ml.) and refluxed for 15 min. The solution was cooled, 0·1N-sodium metaperiodate (10 ml.) added, and the whole made up to 25 ml. Portions (3 ml.) were taken and back titrated in the usual way. Titrations after 1, 2, 6, and 7 hr. indicated that 1·8, 2·6, 3·2, and 3·3 equivalents, respectively, of periodate had reacted.

(*b*) α-Bromotutin (0·208 g.) was hydrolysed and oxidised in a similar way to (*a*). Titrations at 0·75, 1·75, 6, and 9 hourly periods showed uptake of 0·85, 0·9, 1·0, and 1·2 equivalents of periodate, respectively.

(*c*) Tutindicarboxylic acid (0·018 g.) was oxidised with periodic acid and titres, taken after 10 min., 30 min., 1·25 hr., 2 hr., and 4 hr., showed an uptake of 1·3, 2·8, 3·5, 3·5, and 3·8 equivalents of periodate, respectively. A reaction under conditions corresponding to (*a*) showed a similar rate of uptake of oxidant.

(*d*) Tutindicarboxylic acid (0·21 g.) and 0·0331N-lead tetra-acetate in glacial acetic acid (20 ml.) were made up to 50 ml. in a standard flask, with glacial acetic acid, and estimated in the usual way. Titrations after 20, 40, 70, 95, 125, 165, 290, and 325 min. showed an uptake of 1·6, 1·8, 2·1, 2·14, 2·4, 2·6, 2·8, and 2·8 equivalents of oxidising agent, respectively.

Debromination of α-Bromoisotutinone.—(*a*) α-Bromoisotutinone (0·46 g.) was debrominated in the usual way with 3 separate additions of ammonium chloride and zinc dust—the total time of reaction being *ca.* 30 min. The excess of zinc was filtered off and the filtrate taken to dryness. Water (a few ml.) was added with stirring, and after sufficient concentrated hydrochloric acid was added to bring the solution to pH 2 the initial flocculent precipitate dissolved. The solution was kept overnight and the crystals (0·12 g.) were filtered off. The filtrate was continuously extracted with ether; the first 24 hr. yielded material (0·12 g.) which later proved to be identical with the crystalline product above. This was crystallised from water, then ethyl acetate, and sublimed for analysis; the *chloro-acid* (VI) then had m. p. 226° (Found: C, 54·1; H, 5·8; Cl, 10·4. $C_{15}H_{17}ClO_6$ requires C, 54·8; H, 5·2; Cl, 10·8%); $\lambda_{max.}$ (in ethanol) 2540 and 3200 Å (log ε 3·84 and 1·85); $\nu_{max.}$ (potassium chloride disc) 3472s, 1742s, 1727s, 1685s, and 1608m cm.$^{-1}$.

(*b*) The debromination (0·4 g.) was repeated as described above, but the reaction time was cut to 10 min. The solid residue was taken up in a little water and acidified with 2N-sulphuric

[10] H. Conroy, *J. Amer. Chem. Soc.*, 1957, **89**, 5550; B. M. Craven, *Tetrahedron Letters*, 1960, **19**, 21.

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acid and kept overnight. Crystalline material (0·18 g.) was filtered off and after recrystallisation from water, the first crop gave no depression of m. p. when mixed with starting material. From these mother-liquors a second product in very small yield was obtained as short needles, m. p. 238° (constant), and was the *dilactone* (V) (Found: C, 61·8; H, 5·6. $C_{15}H_{16}O_8$ requires C, 61·6; H, 5·5%); $\nu_{max.}$ (potassium chloride disc) **3534s, 1764s, 1704s,** and **1618s** cm.$^{-1}$. Ether extraction of the original filtrate yielded material (0·05 g.), m. p. 224° undepressed when mixed with acid (VI).

Isomerisation of α-Bromotutinone.—α-Bromotutinone (0·42 g.) was dissolved by shaking it for 1 hr. in 1 mol. of 0·1N-sodium hydroxide (the same product was formed from 2 mol. of alkali). The pale yellow solution was acidified with glacial acetic acid, becoming colourless and yielding fine needles which were collected (0·32 g.) and recrystallised from ethanol. The *lactol* had m. p. 218° (decomp.) (Found: C, 46·8; H, 4·3; Br, 20·3. $C_{15}H_{17}BrO_7$ requires C, 46·3; H, 4·4; Br, 20·6%); $\nu_{max.}$ (in Nujol) **3475, 3310, 1756,** and **1741** cm.$^{-1}$. The lactol was dissolved in methanol and treated with diazomethane until a yellow colour persisted. The *methyl ester monomethyl ether* crystallised in fine yellow needles, m. p. 217° (Found: C, 49·2; H, 4·9; Br, 18·8. $C_{17}H_{21}BrO_7$ requires C, 48·9; H, 5·7; Br, 19·1%); $\nu_{max.}$ (potassium bromide disc) **3496, 3443sh,** and **1723br** cm.$^{-1}$.

VICTORIA UNIVERSITY OF WELLINGTON, N.Z.
THE UNIVERSITY OF MELBOURNE,
PARKVILLE, N.2, VICTORIA, AUSTRALIA.

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577. *Polysaccharides from the Green Seaweeds of* Caulerpa *spp. Part III.*[1] *Detailed Study of the Water-soluble Polysaccharides of* C. filiformis: *Comparison with the Polysaccharides Synthesised by* C. racemosa *and* C. sertularioides.

By I. M. MACKIE and ELIZABETH PERCIVAL.

Arabinose, galactose, xylose, and mannose have been separated and characterised from a hydrolysate of a water-soluble extract of *C. filiformis* harvested in November. Fractionation provides evidence for the presence of more than a single polysaccharide in this extract.

Preliminary studies on *C. racemosa* and *C. sertularioides* have established the essential similarity of their polysaccharides with those of *C. filiformis*, though the two former species appear to be devoid of arabinose-containing polysaccharide, and the proportion of starch-type polysaccharide is considerably less than in *C. filiformis*.

A THIRD sample of *C. filiformis* was collected in November in S. Africa from the same site as the two earlier batches of weed which had been harvested in February.[2] The properties of the water-soluble extract (D), from this third batch of weed, and that of the water-soluble polysaccharide (C) [1] separated from the first two samples of weed, are compared in Table 1 (all the figures refer to extracts after removal of the amylopectin-type glucan with salivary α-amylase).

TABLE 1.

	Ash (%)	Sulphate (%)	$[\alpha]_D$	Nitrogen (%)	Approx. molar propns. of sugars: Galactose	Mannose	Xylose	Arabinose
Polysaccharide (C)	14·0	16·4	+10·7°	3	5	2	1	0
Polysaccharide (D)	15·2	17·6	+12·8	2·9	5	2	2	1

No trace of ketose could be found in the hydrolysates of either polysaccharide, but both gave positive tests for 3,6-anhydro-hexoses. It is seen that polysaccharide (D)

[1] Part II, Mackie and Percival, *J.*, 1960, 2381.
[2] Mackie and Percival, *J.*, 1959, 1151.

differs from polysaccharide (C) in that it contains arabinose units. The third sample of weed from which (D) was isolated had been extracted under milder conditions than the earlier samples, and the arabinose might have been lost during extraction of the first two samples though treatment of extract (D) under the conditions used in the earlier extractions failed to remove the arabinose. The individual sugars present in the hydrolysate of polysaccharide (D) were separated on a cellulose column and fully characterised. (The proportions of sugars isolated differed from those determined colorimetrically by Wilson's method, but this is attributed to the difficulty of separating on a cellulose column pure samples of xylose, arabinose, and mannose from mixtures containing these three sugars. At the same time it should be mentioned that the recorded yields are those obtained after extensive purification.) In addition to the sugars given in Table 1 traces of L-rhamnose, ribose, L-fucose, and glucose were separated and tentatively identified. The ribose is considered to have arisen from contaminating nucleic acids.

Application of the standard method devised by O'Neill [3] for the determination of 3,6-anhydro-hexose gave a value of about 1% for this polysaccharide extract.

Fractional precipitation of polysaccharides (D) and (C) with ethanol, acetone, Fehling's solution,[4] cupric acetate,[5] cetyltrimethylammonium hydroxide at various pHs,[6] and cetylpyridinium chloride [6] all yielded precipitates which contained the same proportions of sugars as the original materials. Treatment of an aqueous solution either with potassium chloride solution [7] or with Amberlite IR-400 (OH) resin failed to induce any fractionation. No precipitate was deposited with the former and no absorption of polysaccharide occurred with the latter. Partial fractionation of the free acid polysaccharide (D) was achieved with saturated barium hydroxide.[8] By this means three fractions were obtained (see Table 2). Complete fractionation was not achieved although it seems probable from the partial fractionation that more than a single polysaccharide is present in this extract.

Partial hydrolysis with acid or with taka-diastase failed to yield any oligosaccharides. Although this mixture of enzymes was able to degrade the polysaccharide extract to each of the constituent monosaccharides degradation was incomplete, and the residual polysaccharide material still contained the original mixture of sugar residues and the same proportion of sulphate groups. Evidence that at least some of the sulphate residues are located on the galactose units was provided by the separation of a small quantity of a galactose monosulphate from a partial acid hydrolysate.

The relatively small reduction of periodate by polysaccharides (D) and the presence of each of the sugars in the hydrolysate of the oxopolysaccharide, with possibly a slightly

TABLE 2. *Fractionation by barium hydroxide.*

	Weight (mg.)	Sulphate (%)	$[\alpha]_D$	Sugars (mol. %) Galactose	Arabinose	Xylose	Mannose
Polysaccharide (D) ...	500	17·6	+12·8°	49·4	9·2	18·9	22·5
Fraction 1	128	17·4	+12·6	46·1	6·9	21·5	25·5
,, 2	93	18·1	+12·7	61·3	12·0	13·6	13·1
,, 3	222	18·3	+13·2	62·2	12·1	13·2	12·5

increased proportion of glucose and rhamnose, confirm the complexity of this material. Either it has a highly branched structure or the majority of the units are 1,3′-linked. Indeed a 1,3′-linked xylan and glucan have already been isolated from *C. filiformis* [2] and it is very probable that the xylose- and glucose-containing polysaccharides in extract (D) are the same as those characterised earlier in an alkaline extract. Similarly, by analogy

[3] O'Neill, *J. Amer. Chem. Soc.*, 1955, **77**, 2837.
[4] Chanda, Hirst, and Percival, *J.*, 1951, 1240.
[5] Erskine and Jones, *Canad. J. Chem.*, 1956, **34**, 821.
[6] Scott, *Chem. and Ind.*, 1955, 168; Barker, Stacey, and Zweifel, *ibid.*, 1957, 330.
[7] Smith and Cook, *Arch. Biochim. Biophys.*, 1953, **45**, 232.
[8] Meier, *Acta Chem. Scand.*, 1958, **12**, 144.

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with the sulphated galactans separated from red seaweeds,[9] it is likely that the present galactan consists of 1,3′-linked units carrying sulphate groups at position 4. Mannans hitherto extracted from algæ[10] appear to consist of unsulphated 1,4′-linked residues. From the periodate-oxidation results the present mannan must be different and the majority of the mannose units are either linked to sulphate or are themselves 1,3′-linked. The rotation of the polysaccharides is low ($[\alpha]_D$ +12·8°), indicating that the majority of the glycosidic linkages are β.

Earlier studies on *C. filiformis* revealed that the major polysaccharide synthesised by this green seaweed is a β-1,3′-linked xylan,[2] a result that has been substantiated by Iriki *et al.*[10b] for *C. anceps*. In addition, a water-soluble mixture of polysaccharides was extracted from *C. filiformis* and fractionated into an amylopectin-type glucan and a sulphated mixture containing galactose, mannose, and xylose.[1] Similar extractions of *C. racemosa* and *C. sertularioides* have shown that these two species also synthesise mainly xylans which in the case of *C. racemosa* have been shown from periodate studies to be mainly 1,3′-linked. The water-soluble extracts of *C. racemosa* and *C. sertularioides*, however, contain a much lower proportion of glucose-containing polysaccharide than *C. filiformis*, and they, like the first two samples of *C. filiformis*, are devoid of arabinose-containing polysaccharides. Both these may be seasonal and environmental variations. However, until arabinose-containing polysaccharides have been found in other samples of *Caulerpa* spp. they cannot be regarded as characteristic of this genus of green seaweeds.

Comparison of the polysaccharides synthesised by *Caulerpa* spp. with those of other green algæ reveals some similarities and some major differences. In all cases aqueous extraction has yielded a complex mixture of water-soluble sulphated polysaccharides which have resisted fractionation to homopolysaccharides. *Acrosiphonia centralis*,[11] *Ulva lactuca*,[12] and *Enteromorpha* spp.[13] all yielded aqueous sulphated extracts comprising mainly glucose, xylose, rhamnose, and uronic acid. In contrast there is no indubitable evidence for the presence of uronic acid units in the polysaccharides of *Cladophora rupestris*;[14] and its water-soluble extract consists of L-arabinose, D-galactose, D-xylose, and smaller amounts of D-glucose and L-rhamnose. While *Caulerpa* spp. more closely resemble *Cladophora* spp. in the polysaccharide content of the aqueous extracts they differ from all the other genera of green algæ so far examined in the presence of the β-1,3′-linked xylan as the main polysaccharide constituent. Indeed, even after exhaustive alkaline extraction xylose residues are the major carbohydrate units present in the residual weed. It appears that this polysaccharide is closely integrated into the cell wall of the seaweed and replaces cellulose as the structural polysaccharide, a feature which is in accord with the *X*-ray studies of *Ulva lactuca* and *Enteromorpha* spp. by Cronshaw *et al.*[15]

Experimental

The analytical methods used have been described by O'Donnell and Percival.[11]

Two fresh samples of *Caulerpa filiformis* were collected from the same site as the original sample,[2] the first in February 1958 and the second in November 1959. After removal of most of the colouring matter and mono- and di-saccharides by extraction with 80% aqueous ethanol a second supply of the water-soluble sulphated polysaccharide material (C) was extracted from the weed collected in February 1958 by dilute acid at 70° [2] (yield, 2·7% of dry weight of weed). In contrast, weed collected in November 1959, after aqueous-alcholic extraction, was extracted repeatedly with cold water for 24 hr. periods and the extracts were combined and concentrated (D). Both extracts (C and D) were separately digested twice with salivary α-amylase for 24 hr. to remove all the starch-type glucan [1] and then deproteinised with trichloroacetic acid.[14]

[9] Hirst, *Proc. Chem. Soc.*, 1958, 177.
[10] (*a*) Jones, *J.*, 1950, **3293**; (*b*) Iriki, Suzuki, Nisizawa, and Miwa, *Nature*, 1960, **187**, 82.
[11] O'Donnell and Percival, *J.*, 1959, 2168.
[12] Brading, Georg-Plant, and Hardy, *J.*, 1954, **319**.
[13] Lowe, Ph.D. Thesis, London, 1956.
[14] Fisher and Percival, *J.*, 1957, 2666.
[15] Cronshaw, Myers, and Preston, *Biochim. Biophys. Acta*, 1958, **27**, 89.

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Ionic material was removed from the derived solutions by dialysis, and the polysaccharides (C) (yield 2%) and (D) (yield 0·7%) were precipitated with ethanol as off-white powders. The proportions of sugars present in comparable hydrolysates (N-sulphuric acid for 7 hr. at 100°) were determined by Wilson's method [16] after elution with solvent (1) on a paper chromatogram for 60 hr. These and the properties of the two extracts are given in Table 1.

Quantitative determination of the 3,6-anhydro-hexose in polysaccharide (D) [3] (28·0 mg., 18·6 mg.) gave percentage absorbances at 285 mμ of 0·050 and 0·045 respectively. These correspond to 0·9% and 0·8% of 5-hydroxymethyl-2-furfuraldehyde and 1·2 and 1·1% of anhydro-hexose.

Separation and Characterisation of the Sugars Present in Polysaccharide (D).—The polysaccharide was hydrolysed with N-sulphuric acid at 100° for 8 hr. After neutralisation of the cooled solution with barium carbonate and deionisation with resins the derived syrup (0·52 g.) was separated on a cellulose column which was eluted with butan-1-ol half saturated with water, and the following fractions were collected (R_F values refer to solvent 1 of ref. 11):

Fraction I. A syrup (8·2 mg.), R_F 0·55, $[\alpha]_D$ +7·8°, chromatographically identical with L-rhamnose.

Fraction II. A syrup (3·6 mg.), R_F 0·47, chromatographically indistinguishable from ribose.

Fraction III. A syrup (2·9 mg.), R_F 0·45, with a negative rotation and chromatographically identical with L-fucose.

Fraction IV. Crystalline D-xylose (36·3 mg.), m. p. and mixed m. p. 143°, R_F 0·42, $[\alpha]_D$ +19·6° (*c* 1·0). The derived dibenzylidene dimethyl acetal [17] had m. p. 210° undepressed by admixture with a sample prepared from authentic D-xylose.

Fraction V. A syrup (71 mg.), R_F 0·36, was contaminated with fractions (IV) and (VI). Separation on Whatman No. 3 paper gave a syrup (17·2 mg.) chromatographically indistinguishable from L-arabinose. It had $[\alpha]_D$ +105° (*c* 1·7). The derived benzoylhydrazone had m. p. and mixed m. p. 189°.[18]

Fraction VI. A syrup (72 mg.), R_F 0·36, indistinguishable from D-mannose, had $[\alpha]_D$ +14·2° (*c* 1·2). The derived phenylhydrazone [19] had m. p. and mixed m. p. 196°.

Fraction VII. A syrup (6·5 mg.), R_F 0·31, identical with glucose.

Fraction VIII. Crystalline D-galactose (231·2 mg.), m. p. and mixed m. p. 167°, R_F 0·25, $[\alpha]_D$ +75·5° (*c* 1·1). The derived diethyl mercaptal [20] had m. p. and mixed m. p. 140°.

Fractionation of Polysaccharide (D) *with Saturated Barium Hydroxide.*[8]—Polysaccharide (D) (500 mg.) in water (100 c.c.) was re-cycled six times through a column of Amberlite IR-120 (H) resin (80 c.c.). To the derived acid eluate (pH 3·5), diluted to 1 l. with water, was added dropwise a saturated solution of barium hydroxide until precipitation was complete (precipitate 1). Addition of ethanol (3 vol.) to the dialysed concentrated supernatant solution precipitated the residual polysaccharide. This was redissolved in water (500 c.c.), re-converted into the free-acid, and treated with saturated barium hydroxide. The precipitated polysaccharide (precipitate 2) was removed, and addition of alcohol to the dialysed concentrated supernatant liquid deposited precipitate 3. All three fractions were washed with water to remove contaminating barium hydroxide and vigorously stirred in 6% acetic acid solution. The regenerated polysaccharides were precipitated with ethanol, and the precipitates washed free from acid with ethanol and dried with ether. The properties and relative proportions of the sugars present in each of these fractions are given in Table 2.

Separation of a Galactose Monosulphate from a Partial Acid Hydrolysate.—The polysaccharide (D) (987 mg.) was hydrolysed with 0·25N-sulphuric acid for 1 hr. at 100°. Unhydrolysed polysaccharide and sulphate ions were precipitated from the cooled solution by the addition of barium hydroxide until pH 7·5 was attained. The supernatant solution was passed down a column of IR-4B(OH) resin (200 c.c.) at the rate of about 200 c.c. an hour. The column was washed free from neutral sugars with water (2 l.), and the sugar sulphate eluted from the resin with 2N-ammonia (200 c.c.). Concentration of the eluate at room temperature gave a white solid (4·4 mg.). Chromatography (solvent 3) gave a single spot R_{Gal} 0·32, dark blue

[16] Wilson, *Analyt. Chem.*, 1959, **31**, 1199.
[17] Breddy and Jones, *J.*, 1945, 738.
[18] Hirst, Jones, and Woods, *J.*, 1947, 1048.
[19] Butler and Cretcher, *J. Amer. Chem. Soc.*, 1931, **53**, 4358.
[20] Wolfrom, *J. Amer. Chem. Soc.*, 1930, **52**, 2466.

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with Toluidine Blue spray [21] and dark brown with aniline hydrogen phthalate spray. No spot for free galactose could be detected. Hydrolysis of a portion by N-sulphuric acid for 4 hr. at 100° and chromatography (solvent 3) of the neutralised hydrolysate gave a single spot identical in speed and colour with galactose run as a control.

Enzymic Hydrolysis with "Taka-diastase." [22]—Commercial "taka-diastase," freed from contaminating mono- and oligo-saccharides by dialysis, was incubated at 37° with polysaccharide (D) (199 mg.) in water (250 c.c.) in a dialysis sac in a closed system. Chromatographic examination, after 24 hr., of the concentrated dialysate revealed the presence of arabinose with smaller amounts of galactose, mannose, and xylose. No indication for the presence of oligosaccharides was obtained. After digestion for 7 days, during which the water surrounding the dialysis sac was changed frequently, the residual polysaccharide (104 mg.) was isolated (Found: SO_4^{2-}, 17·9%). The combined dialysates yielded on concentration a syrup (52 mg.) consisting of arabinose, galactose, mannose, and xylose. A hydrolysate of the residual polysaccharide contained all four sugars in the same proportions as the hydrolysate from polysaccharide (D) (paper chromatography, visual examination).

Periodate Oxidation of Polysaccharide (D).—The polysaccharide (0·175 g.) was dissolved in 0·1030M-sodium periodate (50 c.c.). The reduction of periodate was measured on samples (1 c.c.) withdrawn at intervals: [23]

Time (hr.)	0	6	24	48	96
Moles of periodate reduced per $C_6H_{10}O_5$ unit	0	0·145	0·189	0·227	0·236

After 96 hr. 1 mole of periodate was reduced by 686 g. of polysaccharide (it being assumed that the contaminating nitrogen-containing material had no action on the periodate). The oxidation was stopped by addition of an excess of ethylene glycol (10 c.c.). After dialysis, freeze-drying afforded the oxopolysaccharide (108 mg.). Chromatography of the hydrolysate revealed the presence of galactose, mannose, arabinose, xylose, glucose, and rhamnose. The first four of these sugars appeared to be present in the same, and the last two in slightly increased, proportions compared with those of the original polysaccharide. A similar oxopolysaccharide was isolated after oxidation for 14 days.

Preliminary Examination of the Polysaccharides of C. racemosa *and of* C. sertularioides.—Samples of *C. racemosa* (Forsk) Weber-van Bosse var. *clarifera* (Turn.) Weber-van Bosse (29 g.) and *C. sertularioides* (Gmal.) Harv. var. *farlowii* Weber-van Bosse (26 g.) collected in October from dead coral in strong surf on the Gata Islands, have been investigated. Both weeds, after removal of colouring matter with 80% aqueous ethanol, were exhaustively extracted with cold water (500 c.c.) in an atmosphere of nitrogen. Partial removal of contaminating protein with trichloroacetic acid by the method used on the *C. filiformis* extracts was followed by precipitation of the polysaccharides with ethanol (4 vol.). After being washed with ethanol and ether these were dried to cream-coloured powders (0·72 g., 2·5%; 0·91 g., 3·5% yield, respectively). From the residual weeds xylans were extracted with alkali.[2] It was necessary to add ethanol to the acidified alkaline extract from *C. sertularioides* to precipitate the xylan. The yield of xylan from *C. racemosa* was 1 g., *i.e.*, 3·3%, and from *C. sertularioides* was 0·50 g., *ca.* 2·0%.

Both water-soluble extracts had a high sulphate content (*ca.* 20·0%). Chromatography of hydrolysates (N-sulphuric acid, 7 hr. at 100°) revealed the presence of the following sugars:

	Galactose	Glucose	Mannose	Xylose	Rhamnose
C. racemosa	× × × × ×	×	× × ×	× × ×	×
C. sertularioides	× × × × ×	×	× × ×	× × ×	×

× = trace

Hydrolysis of the xylans and chromatographic analysis revealed in *C. racemosa* a trace of glucose and much xylose, and in *C. sertularioides* about half as much glucose as xylose.

Examination of the hydrolysates of the residual weeds after removal of the xylans showed the presence of a large proportion of xylose units together with a small quantity of glucose.

[21] Ricketts, Saddington, and Walton, *Biochem. J.*, 1954, **58**, 532.
[22] Courtois, Kada, and Petek, *Bull. Soc. Chim. biol.*, 1958, **40**, 2031.
[23] Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 196.

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Oxidation of the xylan (323·6 mg.) from *C. racemosa* with 0·103M-sodium periodate (50 c.c.) was carried out at room temperature:

Time (hr.)	0	24	48
Moles of periodate reduced per $C_5H_8O_4$ unit	0	0·120	0·126

The oxidation was complete in 24 hr. and corresponded to the reduction of one mole of periodate for every 8·5 anhydro-xylose units. Slow oxidation subsequently occurred, possibly due to the contaminating protein.[24]

The authors are grateful to Professor E. L. Hirst, C.B.E., F.R.S., for his interest and advice, and to the Institute of Seaweed Research for a maintenance grant (to I. M. M.). They are also pleased to record their gratitude to Dr. A. M. Stephen and Mr. Simons for collecting and drying samples 1 and 2 of *C. filiformis*, to Professor W. E. Isaac and Miss McGillivary for sample 3, and to Dr. L. R. Almodovar for harvesting and classifying the samples of *C. racemosa* and *C. sertularioides*.

Department of Chemistry, University of Edinburgh. [*Received, February 6th*, 1961.]

[24] Bragg and Hough, *Biochem. J.*, 1961, **78**, 11.

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578. *Reactions of Fluorocarbon Radicals. Part XVI.* Photolysis of Some Perhalogenoacetones.*

By R. N. Haszeldine and F. Nyman.

The perhalogenoacetones $CF_2Cl{\cdot}CO{\cdot}CF_2Cl$, $CF_2Cl{\cdot}CO{\cdot}CFCl_2$, $CFCl_2{\cdot}CO{\cdot}CFCl_2$, and $CCl_3{\cdot}CO{\cdot}CCl_3$ have been photolysed alone and in the presence of halogen. The products, accounted for by free-radical mechanisms, suggest that acetones containing a predominance of fluorine are photolysed with carbon–carbon fission as the primary step, whereas those containing a predominance of chlorine are photolysed with carbon–chlorine fission.

The photolysis of perhalogeno-ketones is of interest as a possible source of perhalogenoalkyl radicals. Thus, if photolysis of the ketones $CF_2Cl{\cdot}CO{\cdot}CF_2Cl$, $CF_2Cl{\cdot}CO{\cdot}CFCl_2$, $CFCl_2{\cdot}CO{\cdot}CFCl_2$, and $CCl_3{\cdot}CO{\cdot}CCl_3$ involves a free-radical mechanism, as established for acetone [1] and hexafluoroacetone,[2] the radicals $CF_2Cl{\cdot}$, $CFCl_2{\cdot}$, and $CCl_3{\cdot}$ would become available for further study, *e.g.*:

$$CF_2Cl{\cdot}CO{\cdot}CF_2Cl \xrightarrow{h\nu} CF_2Cl{\cdot}CO{\cdot}CF_2Cl^* \longrightarrow CF_2Cl{\cdot} + CF_2Cl{\cdot}CO{\cdot} \longrightarrow CF_2Cl{\cdot} + CO$$

Perhalogenoacetones containing chlorine could, however, break down by an alternative primary process involving carbon–chlorine fission rather than carbon–carbon fission, *e.g.*:

$$CF_2Cl{\cdot}CO{\cdot}CF_2Cl \longrightarrow CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot} + Cl{\cdot}$$

since it is probable that the C–C and C–Cl bond-dissociation energies in such compounds are comparable. The photolysis would then take a different course from that found for hexafluoroacetone.

Photolysis of 1,3-dichlorotetrafluoroacetone in the vapour phase gives the compounds

* Part XV, *J.*, 1954, 1261. The material of Part XVI was presented in part at the American Chemical Society Meeting, 1957, Abs. 24M.

[1] Steacie, "Atomic and Free Radical Reactions," Reinhold, New York, 1954, Vol. I.
[2] Ayscough, Polanyi, and Steacie, *Canad. J. Chem.*, 1955, **33**, 743; Ayscough and Steacie, *Proc. Roy. Soc.*, 1956, *A*, **234**, 476.

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$CF_2Cl{\cdot}CF_2Cl$ (71%), CF_2Cl_2 (18%), and $CF_2Cl{\cdot}CF_2{\cdot}CF_2Cl$ (8%), and the following reaction scheme is suggested:

$$CF_2Cl{\cdot}CO{\cdot}CF_2Cl \xrightarrow{h\nu} CF_2Cl{\cdot}CO{\cdot}CF_2Cl^* \longrightarrow CF_2Cl{\cdot}CO{\cdot} + CF_2Cl{\cdot}$$
$$CF_2Cl{\cdot}CO{\cdot} \longrightarrow CF_2Cl{\cdot} + CO$$
$$CF_2Cl{\cdot} + CF_2Cl{\cdot} \longrightarrow CF_2Cl{\cdot}CF_2Cl$$
$$CF_2Cl{\cdot} + CF_2Cl{\cdot}CO{\cdot}CF_2Cl \longrightarrow CF_2Cl_2 + CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot}$$
$$CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot} + CF_2Cl{\cdot} \longrightarrow CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot}CF_2Cl$$
$$CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot}CF_2Cl \xrightarrow{h\nu} CF_2Cl{\cdot} + CF_2Cl{\cdot}CF_2{\cdot} + CO$$
$$CF_2Cl{\cdot} + CF_2Cl{\cdot}CF_2{\cdot} \longrightarrow CF_2Cl{\cdot}CF_2{\cdot}CF_2Cl$$

The main product then arises by photolysis involving initial carbon–carbon bond fission, as with acetone or hexafluoroacetone. Formation of dichlorodifluoromethane shows that some of the $CF_2Cl{\cdot}$ radicals attack 1,3-dichlorotetrafluoroacetone by abstraction of chlorine, leaving the $CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot}$ radical; this becomes the source of the 1,3-dichlorohexafluoropropane, by combination of $CF_2Cl{\cdot}$ and $CF_2Cl{\cdot}CF_2{\cdot}$ radicals. The concentration of $CF_2Cl{\cdot}$ radicals is relatively high, whereas that of $CF_2Cl{\cdot}CF_2{\cdot}$ radicals at a given time is low, thus explaining why at most only very small amounts of 1,4-dichloro-octafluorobutane are produced by another radical combination:

$$2CF_2Cl{\cdot}CF_2{\cdot} \longrightarrow (CF_2Cl{\cdot}CF_2)_2$$

The formation of $CF_2Cl{\cdot}$ radicals was also shown by photolysis of the ketone in presence of chlorine, bromine, or iodine, which gave mainly dichlorodifluoromethane (96% yield), bromochlorodifluoromethane (93% yield), or chlorodifluoroiodomethane (57% yield), respectively:

$$CF_2Cl{\cdot}CO{\cdot}CF_2Cl \longrightarrow 2CF_2Cl{\cdot} \xrightarrow{X_2} 2CF_2ClX \ (X = Cl, Br, \text{or } I)$$

The reaction in presence of bromine also gave a low yield of chlorodifluoroacetyl bromide, providing evidence for the existence of the $CF_2Cl{\cdot}CO{\cdot}$ radical as an intermediate:

$$CF_2Cl{\cdot}CO{\cdot}CF_2Cl \longrightarrow CF_2Cl{\cdot} + CF_2Cl{\cdot}CO{\cdot} \xrightarrow{Br_2} CF_2Cl{\cdot}COBr$$

and indicating that the primary photolysis step involves liberation of one, rather than two, chlorodifluoromethyl radicals.

It is unlikely that initial photolysis of the added halogen X_2 facilitates reaction by a change in basic mechanism, *e.g.*, by initial abstraction:

$$X_2 \xrightarrow{h\nu} X{\cdot} \xrightarrow{CF_2Cl{\cdot}CO{\cdot}CF_2Cl} XCl + CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot}$$

since when X = Br or I products such as CF_2Br_2, CF_2I_2, $CF_2Cl{\cdot}CF_2Br$, or $CF_2Cl{\cdot}CF_2I$ would be expected from the further reactions of the $CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot}$ radical.

Photolysis of 1,3-dichlorotetrafluoroacetone in presence of tetrafluoroethylene gave polytetrafluoroethylene and liquid polymers, probably telomers:

$$CF_2Cl{\cdot} + nC_2F_4 \longrightarrow CF_2Cl{\cdot}[CF_2{\cdot}CF_2]_n{\cdot} \xrightarrow{CF_2Cl{\cdot}} CF_2Cl{\cdot}[CF_2{\cdot}CF_2]_n{\cdot}CF_2Cl$$
$$\downarrow CF_2Cl{\cdot}CO{\cdot}CF_2Cl$$
$$CF_2Cl{\cdot}[CF_2{\cdot}CF_2]_n{\cdot}Cl$$

Use of ethylene instead of tetrafluoroethylene similarly gave oils of b. p. 100—200°; infrared spectroscopy showed the presence of carbonyl groups, suggesting initiation or termination reactions involving $CF_2Cl{\cdot}CO{\cdot}$ and/or $CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot}$ radicals, *e.g.*:

$$CF_2Cl{\cdot}CO{\cdot} + CH_2{\cdot}CH_2 \longrightarrow CF_2Cl{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}, \text{ etc.}$$
$$CF_2Cl{\cdot}[CH_2{\cdot}CH_2]_n{\cdot} + CF_2Cl{\cdot}CO{\cdot}CF_2{\cdot} \longrightarrow CF_2Cl{\cdot}[CH_2{\cdot}CH_2]_n{\cdot}CF_2{\cdot}CO{\cdot}CF_2Cl$$

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Photochemical decomposition of 1,1,3-trichlorotrifluoroacetone gave 1,1,2-trichlorotrifluoroethane (21%), 1,2-dichlorotetrafluoroethane (10%), 1,1,2,2-tetrachlorodifluoroethane (10%), and dichlorodifluoromethane (12%):

$$CF_2Cl{\cdot}CO{\cdot}CFCl_2 \xrightarrow{h\nu} CF_2Cl{\cdot} + CFCl_2{\cdot}CO{\cdot}$$
$$CFCl_2{\cdot}CO{\cdot} \longrightarrow CFCl_2{\cdot} + CO$$
(or $CF_2Cl{\cdot}CO{\cdot}CFCl_2 \xrightarrow{h\nu} CFCl_2{\cdot} + CF_2Cl{\cdot}CO{\cdot}$
$CF_2Cl{\cdot}CO{\cdot} \longrightarrow CF_2Cl{\cdot} + CO$)
$$2CF_2Cl{\cdot} \longrightarrow CF_2Cl{\cdot}CF_2Cl$$
$$2CFCl_2{\cdot} \longrightarrow CFCl_2{\cdot}CFCl_2$$
$$CF_2Cl{\cdot} + CFCl_2{\cdot} \longrightarrow CF_2Cl{\cdot}CFCl_2$$

That the yield of 1,1,2-trichlorotrifluoroethane is twice that of the compounds $CF_2Cl{\cdot}CF_2Cl$ and $CFCl_2{\cdot}CFCl_2$ indicates that decarbonylation of a perhalogenoacyl radical, *e.g.*, $CFCl_2{\cdot}CO{\cdot}$, occurs soon after its formation, so that the $CFCl_2{\cdot}$ radical so produced is in a favoured position for combination with the $CF_2Cl{\cdot}$ radical formed in the first step of the ketone photolysis:

$$CF_2Cl{\cdot}CO{\cdot}CFCl_2 \longrightarrow CF_2Cl{\cdot} + CFCl_2{\cdot}CO{\cdot} \longrightarrow CFCl_2{\cdot} + CO$$
$$CF_2Cl{\cdot} + CFCl_2{\cdot} \longrightarrow CF_2Cl{\cdot}CFCl_2$$

Alternatively, the fact that the ratio of $CF_2Cl{\cdot}CF_2Cl : CF_2Cl{\cdot}CFCl_2 : CFCl_2{\cdot}CFCl_2$ is 1 : 2 : 1 can be interpreted by assuming (*a*) formation of $CF_2Cl{\cdot}$ and $CFCl_2{\cdot}$ radicals in equal numbers, without the formation of the $CFCl_2{\cdot}CO{\cdot}$ radical as intermediate, and (*b*) equal rate constants for the three radical–radical combinations.

Dichlorodifluoromethane (12%) and products of high b. p. (25%) are also produced by photolysis of 1,1,3-trichlorotrifluoroacetone. Trichlorofluoromethane is not a major photolysis product, and this implies (i) that the chlorine abstraction

$$CF_2Cl{\cdot} \xrightarrow{CF_2Cl{\cdot}CO{\cdot}CFCl_2} CF_2Cl_2$$

is distinctly faster than the reaction

$$CFCl_2{\cdot} \xrightarrow{CF_2Cl{\cdot}CO{\cdot}CFCl_2} CFCl_3$$

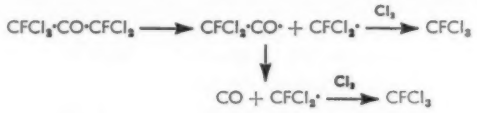
and (ii) that abstraction of chlorine occurs preferentially from the $CFCl_2$ group of 1,1,3-trichlorotrifluoroacetone; this is as expected from the properties and reactions of other compounds containing these groups.

Some of the $CFCl_2$ groups must be involved in formation of the products of high b. p., either by initial carbon–chlorine fission, or by combination with $CF_2Cl{\cdot}CO{\cdot}CFCl{\cdot}$ radicals:

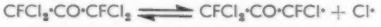
$$CF_2Cl{\cdot}CO{\cdot}CFCl_2 \xrightarrow{h\nu} CF_2Cl{\cdot}CO{\cdot}CFCl{\cdot} + Cl{\cdot}$$
$$CF_2Cl{\cdot}CO{\cdot}CFCl_2 \xrightarrow[CF_2Cl{\cdot}]{} CF_2Cl{\cdot}CO{\cdot}CFCl{\cdot} + CF_2Cl_2$$
$$CF_2Cl{\cdot}CO{\cdot}CFCl_2 \longrightarrow CF_2Cl{\cdot}CO{\cdot} + CFCl_2{\cdot}$$
$$CF_2Cl{\cdot}CO{\cdot}CFCl{\cdot} + CFCl_2{\cdot} \longrightarrow CF_2Cl{\cdot}CO{\cdot}CFCl{\cdot}CFCl_2 \xrightarrow{h\nu} \text{etc.}$$

Photolysis of 1,1,3,3-tetrachlorodifluoroacetone and of hexachloroacetone also suggests that as the percentage of chlorine in these perhalogenoacetones increases, the primary photolysis step changes from predominantly carbon–carbon to predominantly carbon–chlorine fission. Photolysis of 1,1,3,3-tetrachlorodifluoroacetone in presence of chlorine is very slow, and the rate of reaction is much the same as for photolysis in absence of chlorine.

Only trichlorofluoromethane is produced. Presence of chlorine would have facilitated photolysis by carbon–carbon fission, by trapping the radicals produced, *e.g.*:

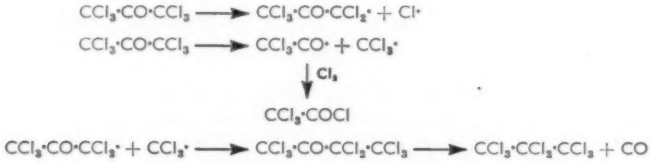


whereas it would inhibit photolysis by carbon–chlorine fission:

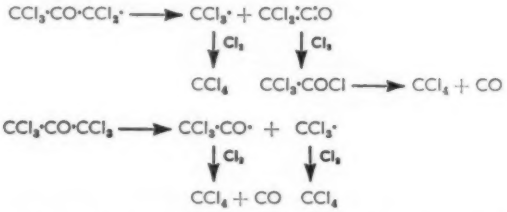


The primary process in photolysis of monochloroacetone has recently been shown [3] to involve carbon–chlorine fission rather than the carbon–carbon fission expected by analogy with acetone, so even one chlorine has a marked influence in ketones that do not contain fluorine.

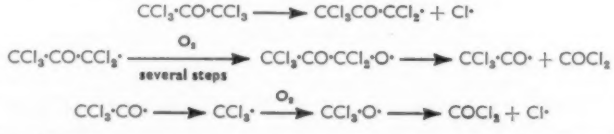
Liquid hexachloroacetone is photolysed only extremely slowly, to give hexachloroethane, octachloropropane, and trichloroacetyl chloride:



whereas photolysis in presence of chlorine, also extremely slow, yields only carbon tetrachloride:



Photolysis of these highly chlorinated acetones is primarily a liquid-phase process (*e.g.*, $CCl_3{\cdot}CO{\cdot}CCl_3$, b. p. 202°), and a combination of " cage-effect " and relatively high stability of radicals such as $CCl_3{\cdot}CO{\cdot}CCl_2{\cdot}$ leading to recombination of the radicals produced in the primary step, may well be responsible for the very slow rates of photolysis, rather than a very difficult primary step. That radical recombination plays a major rôle is suggested by the observation that photolysis of hexachloroacetone in presence of oxygen is considerably faster. Oxygen is known [4] to be a particularly efficient scavenger for perhalogenoalkyl radicals, and to lead to the formation of carbonyl halides; hexachloroacetone similarly yields only carbon dioxide and carbonyl chloride:



[3] Strachan and Blacet, *J. Amer. Chem. Soc.*, 1955, **77**, 5254.
[4] Haszeldine and Nyman, *J.*, 1959, 387, 420, 1084.

The available evidence is thus consistent with a primary step for a highly chlorinated acetone $CXCl_2{\cdot}CO{\cdot}CXCl_2$ (X = F or Cl) involving quite rapid carbon–chlorine fission, but with the equilibrium

$$CXCl_2{\cdot}CO{\cdot}CXCl_2 \rightleftharpoons CXCl_2{\cdot}CO{\cdot}CXCl{\cdot} + Cl{\cdot}$$

lying to the left, whereas the more highly fluorinated acetones, like the corresponding ketones containing only hydrogen, are photolysed by carbon–carbon fission.

Since this work was completed a report has appeared [5] of related studies in substantial agreement with some of the results reported above, but with minor differences in interpretation.

Experimental

The chlorofluoro-ketones, a gift from the Allied Chemical and Dye Corporation, General Chemical Division, U.S.A., were purified by distillation. Gas–liquid chromatography and infrared spectroscopy showed that other chlorofluoro-ketones were absent. Hexachloroacetone was a commercial sample, similarly purified.

General Technique.—Photolyses were carried out in sealed silica tubes. Reactants were either condensed into the evacuated tube, by standard vacuum techniques, or were put into the tube in a fragile glass ampoule which was broken after the reaction tube had been evacuated and sealed. A Hanovia S-250 ultraviolet lamp was used, without the Wood's filter, at 5—15 cm. from the reaction tube. In experiments where the compound to be photolysed was partly in the liquid phase, the reaction vessel was shaken vigorously in a horizontal position so that both liquid and vapour were irradiated simultaneously. Purely thermal reactions during long periods of photolysis were negligible.

The volatile products were transferred to a vacuum-system for distillation and identification. Products (*e.g.*, carbon monoxide) not condensed *in vacuo* by liquid nitrogen were discarded without further examination or were manipulated by use of a Töpler pump. Products with a b. p. too high for convenient manipulation in a vacuum-system were distilled through a vacuum-jacketed semimicro-column. Products were identified by b. p., molecular-weight determination (Regnault's method), analysis, etc., and their identity was confirmed by infrared spectroscopy (Perkin–Elmer model 21 spectrophotometer with sodium chloride optics). Mixtures of products which could not be separated by distillation on the scale employed were analysed by infrared spectroscopy, often combined with molecular-weight determination and, where appropriate, by removal of components of the mixture by chemical reactions, *e.g.*, treatment with mercury to remove free halogen, treatment with aqueous sodium hydroxide to remove compounds such as $COCl_2$, CO_2, COF_2, SiF_4, $CF_2Cl{\cdot}COBr$, $CCl_3{\cdot}COCl$.

Analytically and spectroscopically pure samples of the following compounds were available from other work for reference spectra, etc.: CF_2Cl_2, $CF_2Cl{\cdot}CF_2Cl$, $CF_2Cl{\cdot}CF_2{\cdot}CF_2Cl$, $CF_2{:}CF_2$, COF_2, $COCl_2$, CO_2, $CF_2Cl{\cdot}COBr$, $CCl_3{\cdot}COCl$, CF_2ClBr, CF_2ClI, SiF_4, $CFCl_2{\cdot}CFCl_2$, $CF_2Cl{\cdot}CFCl_2$, CF_3Cl, C_2Cl_6, CCl_4, C_3Cl_8.

Photolysis of 1,3-Dichlorotetrafluoroacetone.—(i) *Alone.* 1,3-Dichlorotetrafluoroacetone (3·384 g., 17·0 mmole) was sealed in a 360 ml. silica tube (ketone entirely in the vapour phase) and exposed to ultraviolet light for 45 hr. The carbon monoxide produced was pumped off, and the volatile products were distilled to give (*a*) an unidentified residue, b.p. >80° (0·053 g.) (Found: C, 16·3%), (*b*) 1,3-dichlorohexafluoropropane (0·308 g., 1·39 mmole, 8%), (*c*) 1,2-dichlorotetrafluoroethane (2·065 g., 12·1 mmole, 71%), and (*d*) dichlorodifluoromethane (0·369 g., 3·0 mmole, 18%).

Irradiation of *liquid* 1,3-dichlorotetrafluoroacetone gave a similar distribution of products ($CF_2Cl{\cdot}CF_2{\cdot}CF_2Cl$ 2%; $CF_2Cl{\cdot}CF_2Cl$ 78%; CF_2Cl_2 3%).

(ii) *In the presence of tetrafluoroethylene.* 1,3-Dichlorotetrafluoroacetone (2·710 g., 13·6 mmole) and tetrafluoroethylene (1·980 g., 19·8 mmole), irradiated in a 320 ml. silica tube for 42 hr., rapidly deposited polytetrafluoroethylene (1·5 g.), and an involatile liquid polymer (0·8 g.). Distillation of the volatile products gave (*a*) 1,3-dichlorohexafluoropropane (0·146 g., 0·66 mmole, 5%), (*b*) 1,2-dichlorotetrafluoroethane (1·150 g., 6·82 mmole, 50%), and (*c*) dichlorodifluoromethane (0·224 g., 2·71 mmole, 20%).

[5] Bowles, Majer, and Robb, *Nature*, 1960, **187**, 314; Bowles, Derbyshire, Majer, and Patrick, *Nature*, 1960, **185**, 683.

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(iii) *In the presence of ethylene.* 1,3-Dichlorotetrafluoroacetone, (2·926 g., 14·7 mmole) and ethylene (0·390 g., 13·9 mmole) were sealed in a 150 ml. silica tube and exposed to ultraviolet light for 40 hr. The volatile products were fractionally distilled *in vacuo*, to give (*a*) 1,3-dichlorohexafluoropropane (0·095 g., 0·43 mmole, 3%), (*b*) 1,2-dichlorotetrafluoroethane (0·420 g., 2·46 mmole, 18%), and (*c*) dichlorodifluoromethane (0·026 g., 0·21 mmole, 2%). The liquid products (2·30 g.) were distilled to give a series of fractions boiling between 54°/23 mm. and 120°/23 mm. Infrared spectroscopy showed that each fraction contained one or more carbonyl groups, but together with analytical data indicated that they were complex mixtures. Further resolution was not achieved on the scale employed.

(iv) *In the presence of chlorine.* 1,3-Dichlorotetrafluoroacetone (1·088 g., 5·46 mmole) and chlorine (0·591 g., 8·32 mmole) in a 150 ml. silica tube were irradiated for 80 hr. The volatile products were shaken with mercury to remove chlorine, transferred to the vacuum-system, then distilled to give unchanged 1,3-dichlorotetrafluoroacetone (0·421 g., 2·12 mmole, 39% recovery), and a mixture shown to consist of dichlorodifluoromethane (0·678 g., 6·43 mmole, 96%) and carbonyl fluoride (0·016 g., 0·25 mmole).

(v) *In the presence of bromine.* 1,3-Dichlorotetrafluoroacetone (0·894 g., 4·50 mmole) and bromine (0·944 g., 5·90 mmole) in a 150 ml. silica tube were exposed to ultraviolet light for 72 hr. The volatile products were shaken with mercury to remove bromine, and distilled *in vacuo* to give unchanged 1,3-dichlorotetrafluoroacetone (0·617 g., 3·10 mmole, 69% recovery), bromochlorodifluoromethane (0·429 g., 2·59 mmole, 93%), and chlorodifluoroacetyl bromide (0·016 g., 0·06 mmole, 4%).

(vi) *In the presence of iodine.* 1,3-Dichlorotetrafluoroacetone (0·755 g., 3·79 mmole) and iodine (1·20 g., 4·70 mmole) were sealed in a 150 ml. silica tube and irradiated for 88 hr. The volatile products, treated with mercury to remove iodine, were chlorodifluoroiodomethane (1·01 g., 4·29 mmole, 57%), dichlorodifluoromethane (0·060 g., 0·50 mmole), and a mixture (0·135 g., 2·5 mmole) of carbon dioxide, carbonyl fluoride and a trace of silicon tetrafluoride.

(vii) *In presence of oxygen.* The ketone (0·410 g., 2·06 mmole) and oxygen (0·513 g., 16·0 mmole), irradiated for 7·5 hr. in a 260 ml. tube (initial pressure *ca.* 2 atm.), gave unchanged ketone (0·100 g., 0·502 mmole, 24%), chlorine (removed by reaction with mercury), and a mixture (0·183 g., 3·09 mmole) of the compounds CO_2, SiF_4, COF_2, and COFCl (trace).

Photolysis of 1,1,3-*Trichlorotrifluoroacetone.*—1,1,3-Trichlorotrifluoroacetone (3·946 g., 18·2 mmole), irradiated in a 360 ml. tube for 47 hr., gave carbon monoxide and (*a*) a fraction containing 1,1,3-trichlorotrifluoroacetone (0·200 g., 0·93 mmole, 5% recovery) and 1,1,2,2-tetrachlorodifluoroethane (0·335 g., 1·64 mmole, 10%), (*b*) 1,1,2-trichlorotrifluoroethane (0·694 g., 3·70 mmole, 21%), and (*c*) a mixture of 1,2-dichlorotetrafluoroethane (0·300 g., 1·75 mmole, 10%) and dichlorodifluoromethane (0·260 g., 2·15 mmole, 12%). The liquid (*ca.* 1·0 g.) boiling in the range 100—200°, which remained in the reaction tube, was not characterised further; spectroscopic examination revealed the presence of keto-groups of the $>CF\cdot CO\cdot CF<$ type.

Photolysis of 1,1,3,3-*Tetrachlorodifluoroacetone in Presence of Chlorine.*—When 1,1,3,3-tetrachlorodifluoroacetone (1·215 g., 5·24 mmole) and chlorine (0·659 g., 9·27 mmole) were irradiated in a 150 ml. silica tube for 19 days, only chlorine (removed by treatment with mercury), trichlorofluoromethane (0·070 g., 0·67 mmole, 67%) and unchanged tetrachlorodifluoroacetone (1·10 g., 4·74 mmole, 91% recovery) were obtained.

Photolysis of Hexachloroacetone.—(i) *Alone.* Hexachloroacetone (2·00 g., 7·85 mmole) in a 150 ml. silica tube was irradiated for 4 months. Carbon monoxide was the only gaseous product. The oily liquid remaining in the tube consisted of unchanged hexachloroacetone (50%), hexachloroethane (30%), octachloropropane (10%), and trichloroacetyl chloride (10%). The more difficult analysis of these products means that the precise yields are open to greater error (±5%) than in the photolysis of the other ketones.

(ii) *In the presence of chlorine.* Hexachloroacetone (3·40 g., 13·3 mmole) and chlorine (1·007 g., 14·2 mmole), irradiated in a 150 ml. silica tube for 9 days, gave chlorine (removed by treatment with mercury), carbon tetrachloride (0·025 g., 0·16 mmole, 12%), and unchanged hexachloroacetone (3·20 g., 12·0 mmole, 90% recovery).

(iii) *In the presence of oxygen.* Hexachloroacetone (0·810 g., 3·17 mmole) and oxygen (0·551 g., 17·2 mmole) in a 320 ml. silica tube were irradiated for 24 hr. The volatile products were shaken with mercury to remove chlorine and distilled to give carbonyl chloride (0·010 g., 0·10 mmole) and carbon dioxide (0·195 g., 4·44 mmole). The less volatile product consisted only of unchanged hexachloroacetone (0·20 g., 0·78 mmole, 25% recovery).

Infrared Spectra.—These were determined on a Perkin–Elmer 21 instrument with sodium chloride optics. Bands (cm.$^{-1}$) observed were:

$CF_2Cl{\cdot}CO{\cdot}CF_2Cl$ (vapour): 2·79w, 5·53s, 7·92s, 8·37vs, 8·67s, 9·36vs, 10·13s, 11·40vs, 11·57s, 12·33s, 13·53m, 14·45m.

$CF_2Cl{\cdot}CO{\cdot}CFCl_2$ (vapour): 2·80w, 5·55s, 8·07s, 8·47vs, 8·90s, 9·24s, 10·43s, 11·67s, 12·27m, 12·74s, 14·05s, 14·60s.

$CFCl_2{\cdot}CO{\cdot}CFCl_2$ (liquid film): 5·60s, 8·38m, 8·54w, 8·97s, 9·19s, 9·35s, 10·55, 10·65m (doublet), 11·20vs, 13·0s, 14·32s, 14·95, 15·00s (doublet).

$CCl_3{\cdot}CO{\cdot}CCl_3$ (liquid film): 5·61s, 5·74m, 8·98m, 11·15s, 11·75, 11·90vs (doublet), 15·13s.

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, February 6th*, 1961.]

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579. *Solid Transitions in Mixed Crystals of Ethylene Dichloride and Ethylene Dibromide.*

By J. E. SPICE, G. A. HARROW, C. R. MCGOWAN, and E. B. SMITH.

Heat capacities have been measured for eight mixed crystals of ethylene dichloride and ethylene dibromide. The solid transitions observed are discussed in terms of the transitions shown by the pure compounds, and of the lattice forces in the mixed crystals. They indicate a solid miscibility gap over the approximate range 5—40 moles % of ethylene dichloride; super-lattices may be formed at low temperatures in crystals with nearly equal proportions of the two constituents.

HEAT capacities give information on the size of lattice forces in crystals, and many qualitative results which bear on the mechanism of solid transitions have been obtained from such studies. Various factors render it difficult to derive more precise information. First, a considerable contribution to the measured C_p (heat capacity at constant pressure) comes from the term β^2VT/α which, although obviously affected by the overall dynamics of the crystal, is not related as directly to the energetics of the crystal as is C_v (the heat capacity at constant volume). Secondly, little work has been done on the theory of the heat capacities of complex crystals. One or two workers [1] have separated C_p for certain compounds into the contributions arising from inter- and intra-molecular motions of various kinds, but the information necessary for this is often lacking. In an alternative approach, the effect is studied of diluting the lattice of a compound which undergoes a phase transition with a second kind of molecule or ion, and observing the effect on the temperature and nature of the transition. The added component has usually been an inert diluent,[2] but a few studies have been made of the transitions occurring in mixed crystals both of whose components exhibit solid transitions.[3] The phenomena in such cases are naturally more complex than for simple dilution.

This paper concerns heat-capacity measurements of mixtures of ethylene dichloride and ethylene dibromide. The dibromide has a first-order transition just below its melting point, while the dichloride has a transition of higher order at a fairly low temperature.

[1] Lawson, *Phys. Rev.*, 1940, **57**, 417; Marshall, Staveley, and Hart, *Trans. Faraday Soc.*, 1956, **52**, 19.
[2] Eucken and Veith, *Z. phys. Chem.*, 1936, *B*, **34**, 275.
[3] Bartholomé, Drikos, and Eucken, *Z. phys. Chem.*, 1938, *B*, **39**, 371; Mandleburg and Staveley, *J.*, 1950, 2736.

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The two compounds form a continuous series of mixed crystals,[4] so that heat capacity measurements should throw light on the forces affecting each kind of molecule.

Experimental

Calorimeter and Auxiliary Apparatus.—The calorimeter assembly used for most of the measurements (calorimeter II) was closely similar to that of Aston and Ziemer.[5] The calorimeter vessel was of about 70 c.c. capacity, and was suspended inside a cylindrical copper " mantle," with conical ends, which itself hung from a lead block. This block was suspended from a circular plate to which were soldered the outer brass can and the main pumping tube, which also carried the electrical leads. During measurements the outer can and the mantle were continuously evacuated. The whole assembly was immersed either in a mixture containing solid carbon dioxide or in liquid nitrogen, according to the temperature range. The three portions of the mantle carried heating coils, by means of which its temperature could be kept equal to that of the calorimeter vessel. Copper–constantan thermocouples showed differences of temperature between the mantle and the calorimeter vessel. The coil heating the calorimeter was wound in a shallow inset in the outer face of a hollow copper cylinder, which was a push-fit in the axial well of the calorimeter vessel; it was of 44 S.W.G. constantan, and had a resistance of 120 ohms at room temperature. The platinum resistance thermometer consisted of two resistance elements, contained in a platinum capsule 7 cm. long and 6 mm. in outside diameter; [6] this fitted tightly inside the copper cylinder carrying the heating element. Each thermometer element was made by winding about 150 cm. of 48 S.W.G. " thermopure " platinum wire on a 1 mm. steel mandrel in a lathe, and then drawing it out to form a fairly close spiral, which was supported in a thin Pyrex tube, 2 mm. in outside diameter. Thicker platinum leads were soldered to the ends of the elements and brought out through a bulb of lead glass, fused to the open end of the platinum sheath. The complete thermometer was filled with helium to a pressure of 0·5 atm. at room temperature; it had a resistance of 69·3 ohms at 0°. After careful annealing, the thermometer was calibrated by measuring its resistance at the ice-point and at the b. p.s of naphthalene, water, and liquid oxygen. From these results the four constants of the International Temperature Scale were determined, and deviation graphs were plotted so as to permit the accurate calculation of temperatures from a linear function of the thermometer resistance. A double potentiometer was used for the measurement of both temperature and energy input, in the usual manner. The galvanometer sensitivity was such that with a lamp-scale distance of two m., a spot deflection of 1 cm. corresponded to a temperature change of 0·001°.

The determination of heat capacities and heats of fusion followed the standard procedure. Away from the region of a transition, thermal equilibrium was rapidly attained, but within the transition region conditions were more sluggish, and an hour might elapse between the end of a heating period and the re-attainment of a steady temperature drift. With care, the temperature of the calorimeter could be made to change by as little as 0·001° in five min., and heat-capacity determinations were usually made under these conditions.

For the earlier measurements a glass calorimeter (calorimeter I) was employed, consisting of a cylindrical Pyrex vessel of about 80 c.c. capacity, with a combined resistance thermometer–heater of 40 S.W.G. platinum wire wound directly on it. This had a resistance of ~175 ohms at room temperature. The calorimeter vessel was suspended inside a brass mantle fitted with a heating coil, and this in turn was freely suspended inside a continuously evacuated outer vessel, immersed in the cooling medium. Thermocouples showed the difference in temperature between the calorimeter and its surroundings. The electrical measurements and general experimental procedure were the same as for calorimeter II. Calorimeter I gave quite accurate results except in transition regions, where the glass calorimeter and external thermometer were ill-adapted for following sluggish transformations requiring considerable time.

Materials.—Ethylene dibromide was washed with concentrated sulphuric acid and then with dilute sodium carbonate, dried ($CaCl_2$), and kept over phosphorus pentoxide for a week. It was distilled from mercury through a 12" Dufton column, and the fraction boiling above 130·5° was then fractionated over anhydrous sodium sulphate, through a 120 cm. column

[4] Timmermans, *Bull. Soc. chim. belges*, 1927, **36**, 186.
[5] Aston and Ziemer, *J. Amer. Chem. Soc.*, 1946, **68**, 1405.
[6] Barber, *J. Sci. Instr.*, 1950, **27**, 47.

packed with Fenske helices and with a reflux ratio of 50 : 1. For the final sample $n_D^{15} = 1{\cdot}54160$, agreeing with the value quoted by Timmermans.[7]

Ethylene dichloride was washed with 5% aqueous potassium hydroxide and then with water and dried ($CaCl_2$ overnight; P_2O_5 for a week), then fractionated over anhydrous sodium sulphate in the 120 cm. column at a reflux ratio of 50 : 1. The fraction of b. p. 83·5° had n_D 1·44756 (lit.,[7] 1·44759). Determination of the melting range showed the sample to contain only 0·03 mole % of liquid-soluble solid-insoluble impurity.

The purified samples were sealed in Pyrex tubes, out of contact with moisture. For further data on purity see below.

Accuracy and Reproducibility of the Measurements.—The heat capacity of the empty calorimeter II was measured over the range 80—300° K. The mean deviation of the experimental points from the best smooth curve through them was ±0·1%, which represents the inherent reproducibility of the calorimetric measurements. As regards absolute accuracy, the following Tables, showing the results obtained in the present work and those of previous workers, indicate that no large systematic errors are likely to affect the accuracy.

Heat Capacities.—Harrow, using calorimeter I, obtained values for ethylene dibromide over the temperature range 170—280° about 1% lower than those reported by Pitzer.[8] Five measurements were made by Smith (calorimeter II) on ethylene dichloride, over the range 220—250° K. The average deviation from Pitzer's values was +0·7%.

Melting Points and Transition Points.—The values obtained in the present work are compared in Table 1, with those reported previously.

Heats of Fusion and Transition.—The results are shown in Table 2.

TABLE 1. *Melting and transition points.*

	$C_2H_4Cl_2$	$C_2H_4Br_2$	
	M. p. (K)	M. p. (K)	Trans. pt. (K)
White and Morgan [a]		249·0°	282·3°
Morino [b]		248·4	
Le Blanc and Mobius [c]			283·07
Timmermans [4]	237·6°	249·1	283·10
Railing [9]	237·65	250·6	283·0
Pitzer [8]	237·2 ± 0·1	249·55 ± 0·1	283·0
Harrow (cal. I)	237·5 ± 0·2	249·6 ± 0·2	282·9 ± 0·2
McGowan (cal. II)	237·60 ± 0·05	249·65 ± 0·05	
Smith (cal. II)	237·65 ± 0·05		

[a] White and Morgan, *J. Chem. Phys.*, 1937, **5**, 655. [b] Morino, *J. Chem. Soc. Japan*, 1939, **60**, 222.
[c] Le Blanc and Mobius, *Ber. Verhandl. Sachs. Akad. Wiss. Leipzig, Math. Phys. Klasse*, 1933, **85**, 75.

TABLE 2. *Heats of fusion and transition.*

Heat of fusion (cal./mole) of $C_2H_4Cl_2$		Heat of transition (cal./mole) $C_2H_4Br_2$	
Railing [9]	2090 ± 21	Pitzer [8]	463·8
Pitzer [8]	2112 ± 2	Harrow (cal. I)	460·7 ± 3
Smith (cal. II)	2106 ± 4		

From all these comparisons the results with calorimeter II appear reliable within ~0·5% (their internal consistency was considerably better). Calorimeter I was less adaptable, but its absolute accuracy was quite good. For following closely the progress of slow thermal transitions, however, calorimeter II was very much better than calorimeter I.

RESULTS

Eight mixtures were investigated, which contained severally 3, 8, 18, 43·5, 51, 60, 80, and 90 moles % of ethylene dichloride. At a given temperature, the heat capacity of the empty calorimeter was subtracted from the total heat capacity of the calorimeter and its contents, and the result was divided by the total number of moles of both components, so as to give a mean molar heat capacity.

Ethylene dichloride and dibromide form a complete series of mixed crystals (at least just

[7] Timmermans and Martin, *J. Chim. phys.*, 1928, **25**, 411.
[8] Pitzer, *J. Amer. Chem. Soc.*, 1940, **62**, 331.
[9] Railing, *J. Amer. Chem. Soc.*, 1939, **61**, 3349.

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below the melting curve) whose melting temperatures lie between the m. p. of the pure components. Since the mixtures had to be made as liquids, there was the possibility that, on cooling, phase separation might occur, to give an inhomogeneous solid consisting of mixed crystals of various compositions. The liquid mixtures were therefore frozen as rapidly as possible, and normally a mixture was not allowed to melt again until all the measurements on it had been completed. A few determinations were made on the same mixture before and after melting, and it was found that, provided the annealing procedure about to be described had been carried out, the results agreed to within the usual experimental uncertainty. Until the importance of careful annealing was realised, extremely erratic results were obtained. It was impossible to reproduce transition temperatures to within closer limits than ~1° and small transitions sometimes appeared. In investigating solid transitions it is always necessary to guard against supercooling, and for the present system—where, as will be seen, phenomena are more complex than usual—this was particularly important. The following cooling and annealing procedure was found satisfactory. Each liquid mixture was cooled as rapidly as possible, by admitting hydrogen to the outer calorimeter spaces and bringing a large vessel of liquid nitrogen suddenly around the calorimeter can, to well below the temperature of the lowest transition for that mixture. It was then heated to within a few degrees of its melting temperature and held

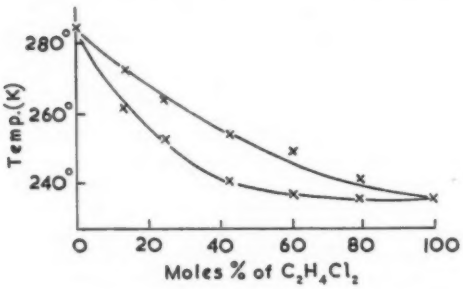


FIG. 1. *Freezing and melting diagram of mixtures of ethylene dichloride and dibromide.*

there for some hours. The calorimeter was next cooled very slowly to below the lowest transition. After the calorimeter and contents had been taken through this heating and cooling cycle three times, reproducible specific-heat curves were obtained over the region of any transition. With a properly annealed crystal the same heat capacity points could be obtained after the mixture had been taken through a transition and then cooled below it again, or after melting the mixture and then freezing and annealing it again. Nevertheless, as much as possible of any transition region was always covered by continuous working.

Fig. 1 is the phase diagram for ethylene dichloride–ethylene dibromide, as obtained by Timmermans;[4] Figs. 2—11 show the variation of the mean molar heat capacity C_p with the absolute temperature, for the pure compounds[8] and for the eight mixtures. All the results shown for mixed crystals were obtained with calorimeter II, except that for 90% ethylene dichloride. The 3% mixture was investigated also in calorimeter I, the curve obtained being virtually identical with that shown. The remaining results from calorimeter I were later confirmed with calorimeter II as regards the temperatures of transitions, but more detail was revealed. Such remaining mixtures were in the intermediate region (10—60 moles % of ethylene dichloride), and calorimeter I possessed insufficient " resolving power " to reveal the full complexity of the heat capacity curves for such compositions. On each curve the melting temperature for that mixture is indicated.

For the discussion of these results, it is convenient to distinguish four temperature ranges:

(A) *Around* 250° K. Ethylene dibromide undergoes a sharp transition at 250° K, which also appears (though at slightly lower temperatures) for the mixtures containing 3, 8, and 18 moles % of ethylene dichloride.

(B) 225—235° K. For the mixtures with 8 and 18 moles % of dichloride, this is a region of complexity, with two or three maxima in the heat capacity curve.

(C) 205—218° K. Mixtures containing 18—60 moles % of ethylene dichloride have a marked, narrow, maximum heat capacity at ~206° K, with a much smaller subsidiary peak ~10° higher.

(D) *Below* 178° K. Ethylene dichloride has a very broad hump in its heat capacity curve, with a maximum at ~178° K. On addition of dibromide the height of this hump is reduced, while its breadth is more or less unaffected. For 90 and 80 moles % of dichloride the hump is as sharp as for the pure dichloride; for the mixtures with 43·5—60 moles % of dichloride, it is appreciably more rounded. The temperature of the maximum is first depressed by addition of dibromide, but with increasing amounts again rises slightly.

FIGS. 2—11. *Heat-capacity curves.* TP = *Transition temperature,* MP = *melting temperature. For* A, B, C, D *see text.*

FIG. 2: Pure $C_2H_4Br_2$.

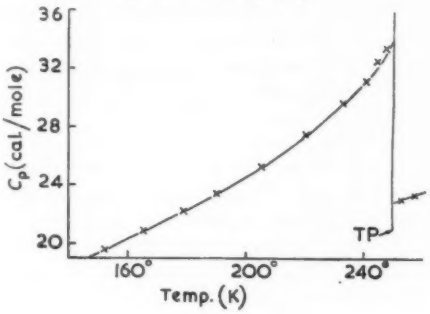


FIG. 3: 3 Moles % of $C_2H_4Cl_2$.

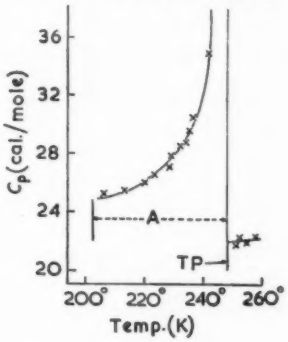


FIG. 4: 8 Moles % of $C_2H_4Cl_2$.

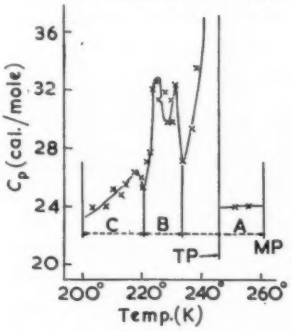


FIG. 5: 18 Moles % of $C_2H_4Cl_2$.

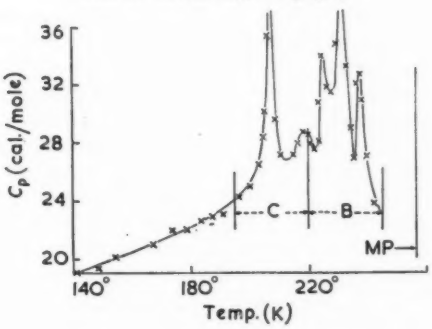


FIG. 6: 43·5 Moles % of $C_2H_4Cl_2$.

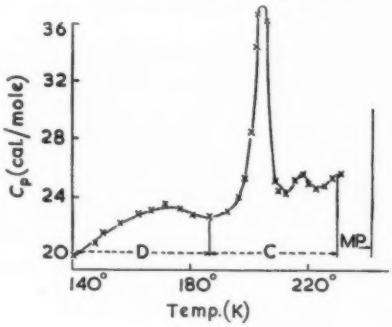


FIG. 7: 51·0 Moles % of $C_2H_4Cl_2$.

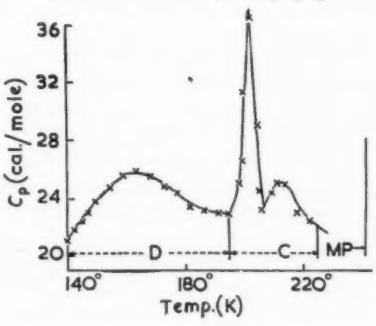


FIG. 8: 60·0 Moles % of $C_2H_4Cl_2$.

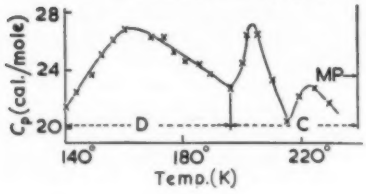


FIG. 9: 80·0 Moles % of $C_2H_4Cl_2$.

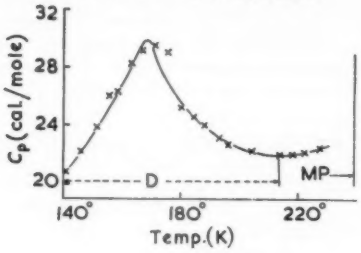


FIG. 10: 90·0 Moles % of $C_2H_4Cl_2$.

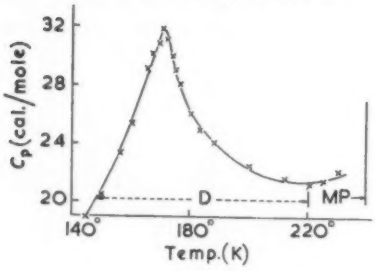
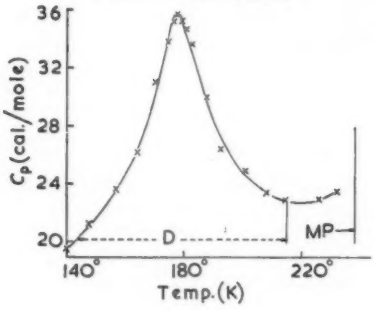


FIG. 11. Pure $C_2H_4Cl_2$.



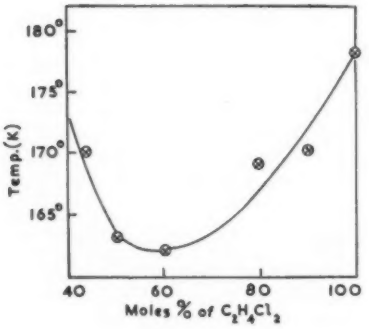


FIG. 12. *Variation of ethylene dichloride transition temperature with composition.*

DISCUSSION

Ethylene dichloride crystallises with a monoclinic space lattice containing two molecules per unit cell.[10] Infrared measurements [11] show the molecules to be in the *trans*-configuration, and *X*-ray and proton magnetic resonance results [12] indicate that the gradual transition at 178° K marks the onset of free rotation of the ethylene dichloride molecules without change of crystal structure. Ethylene dibromide has the same "β" crystal structure as the dichloride above its sharp transition at 250° K, but a different "α" form, also monoclinic but with four molecules per unit cell, below this temperature.[13] The

[10] Milberg and Lipscomb, *Acta Cryst.*, 1951, **4**, 369; Reed and Lipscomb, *ibid.*, 1953, **6**, 45.
[11] Brown and Sheppard, *Trans. Faraday Soc.*, 1952, **48**, 128.
[12] Gutowsky and Pake, *J. Chem. Phys.*, 1950, **18**, 162.
[13] Meerman, Thesis, University of Utrecht, 1943.

dibromide molecules have the *trans*-configuration and are probably rotating as a whole, above 250° K.[11,14]

The sharp transition in pure ethylene dibromide is preceded by a seemingly anomalous rise in heat capacity, which Pitzer [8] suggested was the preliminary stage of a dichloride-type second-order rotational change. This change was more difficult for the dibromide than for the dichloride, was therefore delayed to a higher temperature, and before its completion gave place to a radical lattice change. In the light of the present information on crystal structures, which was not available to Pitzer, the only valid conclusion is that rotation is more difficult in the α dibromide lattice than in the β dichloride lattice.

Timmermans's observations of a continuous series of mixed crystals of ethylene dichloride and dibromide just below the freezing point is reasonable in the light of the crystal structures; although he did not report it, phase separation should occur at lower temperatures, to give a solid miscibility gap. When a mainly dibromide mixed crystal is cooled it will certainly undergo a lattice change at a temperature near that for pure dibromide, and at lower temperatures the dichloride molecules will be in an " alien " lattice. For a mainly dichloride mixed crystal there will be no such lattice change, and the dibromide molecules will always be in a lattice which is the stable one for dibromide at high enough temperatures. The solubility of dibromide in dichloride should therefore be considerably higher than that of dichloride in dibromide.

A further possibility is the formation of a super-lattice, most probably for mixed crystals with more or less equal proportions of each component. There might then be a Curie point, when the ordered low-temperature form passed into the disordered high-temperature form.

Because of these possible complications, only small additions of dibromide to pure dichloride, or *vice versa*, are likely to have a simple effect on phase transitions. Such replacement of the major component will change the lattice spacing and modify the lattice forces. The change in lattice forces will be due to (i) the attendant change in lattice spacing, (ii) the less symmetrical force field in the mixed crystal, and (iii) an actual change in intermolecular forces for a given distance. If the intermolecular forces are mainly dispersion forces they will be larger, the larger the molecules. If, however, carbon–halogen bond dipole attractions make an important contribution, replacement of dichloride by dibromide may result in a net reduction in intermolecular forces. The effect even of small replacements cannot, therefore, be readily predicted.

Region A (~250° K).—If ethylene dichloride were soluble in the high-temperature β-form of the dibromide (which has the same crystal structure) but insoluble in the low-temperature α-form, small additions of dichloride should lower the dibromide transition temperature according to the equation: $\Delta T = RT^2 n_2/n_1 \Delta H$. This would indicate a lowering of about 8° for addition of 3 moles %, as against the observed lowering of less than 2°. The dichloride must, therefore, have a slight solubility in the low-temperature crystal, so that the above equation does not apply. The less symmetrical force-field in the mixed crystal should facilitate lattice transformation, which may not now be strictly isothermal. In fact, experiment shows it to be less sharp than in pure dibromide, as well as occurring at lower temperatures.

Region D (<178° K).—The unusual broadness of the rotational transition in pure ethylene dichloride presumably means that the forces opposing rotation are small, so that no drastic loosening of the inhibiting force-field occurs when the first few molecules begin to rotate. The dependence on composition of the temperature of the " dichloride " transition is shown in Fig. 12. The lowering of the transition temperature from 100 to 60 moles % of dichloride indicates a decrease of lattice forces when dichloride is replaced by dibromide, presumably because the reduction in dipole attractions outweighs the larger dispersion forces expected. The rise in transition temperature for less than 60

[14] Ichishima and Mizushima, *J. Chem. Phys.*, 1950, **18**, 1420.

moles % of dichloride, and the accompanying change in the nature of the heat capacity anomaly, will be discussed in the next section in terms of super-lattice formation.

Region C (205—218° K).—The interconnected peaks near 210° K occur for neither of the pure compounds. They are unlikely to be due to straightforward rotational processes, since they have a shape and composition-dependence different from those of the peak in dichloride-rich mixtures. It is therefore suggested that the maximum at 206° K is due to a super-lattice transformation, which might occur in a molecular crystal when there has been a preliminary acquirement of rotational freedom. Any super-lattice anomaly will be most marked with roughly equimolecular mixtures, since the difference between ordered and disordered structures will then be greatest; so it is significant that the 206° peak is found only for mixtures with 40—60 moles % of dichloride and for the 18% mixture (discussed in the next section). Both its shape and its small dependence of temperature on composition are broadly similar to these factors for super-lattice changes in alloy systems.[15]

On this basis mixtures with more than 60 moles % of dichloride, with no peak at 206° K, have an essentially random arrangement of the two kinds of molecule at all temperatures, and the dichloride transition then almost certainly involves both kinds of molecule. With 40—60 moles % of dichloride there is a super-lattice at low temperatures, and the mutual isolation of the dichloride molecules, with relatively small coupling between them, may account for the facts that the dichloride transition temperature rises again in this range of composition and that the anomaly becomes smaller and more rounded in shape. It may even, in these circumstances, involve only dichloride molecules, or at least only a proportion of the dibromide molecules. In this case, desegregation as a result of the 206° K transition could conceivably facilitate the rotation of any non-rotating dibromide molecules and thus cause the smaller, subsidiary peak about 10° higher.

Region B (225—235° K).—The complex behaviour in this region for mixtures with 8 and 18 moles % of ethylene dichloride is best explained by the existence of a solid miscibility gap. If this gap is between ~5 and ~40 moles % of dichloride, mixed crystals falling outside these limits should remain homogeneous on cooling. Crystals of intermediate compositions should, however, separate into two components, with ~5 and ~40 moles % of dichloride. When such a mixture was heated, it would display the following features: (*a*) A transition or transitions around 210° K for the 40 moles % component, which might also show a dichloride-type transition at a lower temperature. The latter might well be undetectable, since it is only just apparent for the 43·5 moles % mixture. (*b*) One or more maxima, due to energy absorption on remixing to give a homogeneous mixed crystal. (*c*) A dibromide-type transition, at a temperature appropriate either to the homogeneous mixed crystal, or to a separated dibromide-rich component.

The critical (solid) solution temperature might well be just below the melting curve for the system, so that process (*a*) should certainly take place before any remixing. Processes (*b*) and (*c*), however, might occur at about the same temperature, so that here the picture would be more confused.

The complete separation and remixing hitherto assumed would probably not take place, but the annealing procedure should produce at least partial segregation into two mixed crystals, possibly in domains of limited extent, and there would then be some degree of remixing across the domain boundaries on heating. The course of events would then be more complex than already discussed, and several maxima might appear for process (*b*).

In fact, the mixture with 18 moles % of dichloride has peaks at 212° and 218° K, corresponding to those for the middle-range compositions. They are smaller than for the 44 moles % dichloride mixture, presumably because of the small amount of this component in the partially separated mixed crystals. Whether the isolated 216° K peak for 8 moles %

[15] Sykes and Wilkinson, *J. Inst. Metals*, 1937, **61**, 223.

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of dichloride is also due to a 40% component is more doubtful. This mixture has an unmistakable dibromide-type transition at 247° K, which is probably due to a 5 moles % component since it is only slightly lower than that for the 3 moles % mixture. That the 18 moles % mixture shows no dibromide-type peak is possibly because its melting temperature is lower than the expected dibromide transition temperature, even for a 5 moles % crystal. Confidence is therefore felt in attributing the broad features of the heat capacity curves for 8 and 18 moles % mixtures to a partial separation into two mixed crystals, even though it is impossible to analyse these curves in detail.

Summary.—Solid ethylene dibromide can dissolve up to about 5 moles % of ethylene dichloride. For less dichloride than this, the temperature of the sharp ethylene dibromide transition at 250° K is lowered, and the transition becomes less sharp, probably because the force-field in the mixed crystals is less symmetrical than in the pure dibromide.

Solid ethylene dichloride, on the other hand, can dissolve up to about 60 moles % of ethylene dibromide. Up to about 40 moles % of dibromide the replacement is random. The smaller dipole–dipole forces and larger lattice distances which result from the introduction of dibromide then progressively lower the temperature of the broad ethylene dichloride anomaly, though the heat-capacity maximum is as sharp as in pure dichloride. The anomaly is caused by the gradual onset of rotation of ethylene dichloride molecules in the pure compound, and of both kinds of molecule in the mixed crystals. From 40 to 60 moles % of ethylene dibromide, however, a super-lattice may be formed at low temperatures, and the mutual segregation of the two kinds of molecule may then account for the rise in the temperature of the dichloride transition as the proportion of dibromide increases. In this same composition range, the more rounded heat-capacity maximum may indicate that the onset of rotation now concerns only the ethylene dichloride molecules present. The heat-capacity maximum at about 206° K for mixtures in the 40—60 moles % range probably accompanies a super-lattice transformation, and above this temperature the distribution of ethylene dichloride and dibromide molecules is random. The small peak about 10° higher may be associated with the acquiring of rotational freedom by the ethylene dibromide molecules in the disordered crystals.

Finally, the existence of a solid miscibility gap at 5—40 moles % of ethylene dichloride results in the separation into two mixed crystals, containing respectively ~5 and ~40 moles % of ethylene dichloride, when crystals with overall compositions within this range are cooled. On heating, such systems display transitions characteristic of both the 5 and the 40 moles % crystals, and also additional heat-capacity maxima, which probably accompany a complete or partial remixing.

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Department of Inorganic and Physical Chemistry,
University of Liverpool.
[Present addresses: (J. E. S.) Science School, Winchester College,
Winchester, Hants.
(G. A. H.) Thornton Research Centre, Shell Refining Co.,
Ellesmere Port, Cheshire.
(C. R. McG.) Windscale Factory, U.K.A.E.A., Cumberland.
(E. B. S.) Physical Chemistry Laboratory, The University,
South Parks Road, Oxford.] [*Received, March 7th,* 1960.]

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580. *The* ortho : para-*Ratio in Aromatic Substitution. Part I. The Nitration of Methyl Phenethyl Ether.*

By R. O. C. Norman and G. K. Radda.

Methyl phenethyl ether, like anisole and acetanilide, has been found to give a far higher proportion of the *o*-nitro-derivative when nitrated with acetyl nitrate than when nitric acid or mixed acid is the reagent. Evidence has been obtained that acetyl nitrate, and other acyl nitrates, do not themselves bring about nitration of the aromatic compound but give rise to dinitrogen pentoxide. This then reacts in two ways: by heterolysis to the nitronium ion, which brings about nitration at the *ortho*-, *meta*-, and *para*-positions in the same proportions as nitric acid; and by reaction at the oxygen atom of methyl phenethyl ether to form an oxonium ion which rearranges, through a six-membered cyclic transition state, to the *o*-nitro-derivative.

Although the factors which govern rates of aromatic substitution at the *meta*- and *para*-positions of monosubstituted benzenes are relatively well understood,[1,2] little is known about the factors which determine the *ortho* : *para*-ratio in these reactions. This is because it is difficult to estimate quantitatively the effect of steric hindrance to substitution at the *ortho*-position. That steric hindrance is important has been established in certain cases (*e.g.*, in the nitration of t-butylbenzene [3]), but the *ortho* : *para*-ratio is often greater than the statistical value of 2 : 1, indicating that any steric hindrance is outweighed by some more powerful effect. In this paper we report the first results of a study of the factors which determine the *ortho* : *para*-ratio in substitution when this ratio is greater than the statistical value.[4]

It is well known that anisole and acetanilide give rise to higher proportions of *o*-nitro-derivative when nitrated with acetyl nitrate than when nitric acid or mixed acid is the reagent.[5-7] Various tentative explanations of this have been advanced, but none is satisfactory. It has been suggested that the change in orientation may be due to a change in the nitrating species,[8] but this seems unlikely because toluene forms *o*- and *p*-nitro-derivatives in the same proportions with acetyl nitrate as with nitric acid,[6] which indicates that the species responsible for nitration is the same in each case. This follows from the fact that different reagents would almost certainly have different selectivities.[9] Paul has attributed the change in orientation to an electrostatic effect.[10] In anisole, the dipole of the aromatic C–O bond has its negative end towards carbon, resulting in the *ortho*-position's being negatively polarised with respect to the *para*-position, while in chlorobenzene and bromobenzene the corresponding dipole is towards the halogen atom, the *ortho*- being more positively polarised than the *para*-position. This produces an electrostatic attraction between the reagent and the *ortho*-carbon in anisole, aiding *ortho*-substitution, and a repulsion in the halogenobenzenes, retarding *ortho*-substitution. In solvents of low dielectric constant this electrostatic influence is relatively more important, and results in the observed change in orientation. However, the isomer ratios obtained by Paul for the nitration of chlorobenzene and bromobenzene are at variance with the values obtained

[1] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953.
[2] de la Mare and Ridd, "Aromatic Substitution," Butterworths Scientific Publ., London, 1959.
[3] Nelson and Brown, *J. Amer. Chem. Soc.*, 1951, **73**, 5605.
[4] Norman and Radda, *Proc. Chem. Soc.*, 1960, 423.
[5] Griffiths, Walkey, and Watson, *J.*, 1934, 631.
[6] Halvarson and Melander, *Arkiv Kemi*, 1957, **11**, 77.
[7] Holleman, *Chem. Rev.*, 1925, **1** 187; Arnall and Lewis, *J. Soc. Chem. Ind.*, 1929, **48**, 159T.
[8] Ref. 2, p. 76.
[9] Nelson, *J. Org. Chem.*, 1956, **21**, 145.
[10] Paul, *J. Amer. Chem. Soc.*, 1958, **80**, 5332.

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by other workers.[11,12] Moreover, Paul's view that the electrostatic effect is enhanced in solvents of low dielectric constant is contraverted by the fact that the nitration of anisole in acetic acid,[5] which has a lower dielectric constant than acetic anhydride (the usual solvent for reactions with acetyl nitrate), gives the same isomer distribution as nitric acid. Halvarson and Melander [6] suggested that the high *ortho* : *para*-ratio in the nitration with acetyl nitrate might be due to initial attack of the nitrating species at oxygen, followed by an intramolecular rearrangement to the *o*-nitro-compound. They viewed this as an attractive but unlikely explanation.

Two problems arise from these data: first, to discover the nature of the nitrating species in solutions of acetyl nitrate; and secondly, to find whether the observed high *ortho* : *para*-ratios result from the presence in the molecule of an atom with an unshared pair of electrons bonded to the benzene nucleus. We chose to examine the nitration of methyl phenethyl ether, $Ph{\cdot}CH_2{\cdot}CH_2{\cdot}OMe$, since this compound contains an oxygen atom not bonded to the benzene ring. It is also more suitable than anisole in that its reactivity in nitration is not likely to be complicated by nitrosation, and that cleavage of the CH_3–O bond is not so easy in an aliphatic as in an aromatic ether.

None of the three nitro-derivatives of methyl phenethyl ether has previously been reported. The *p*-nitro-compound was readily prepared from *p*-nitrophenethyl bromide, but attempts to make the *o*- and the *m*-nitro-isomer through the corresponding nitrophenylacetaldehydes were unsuccessful because Darzens condensations with the nitrobenzaldehyes gave glycidic acids that formed polymers under the conditions necessary for decarboxylation. The nitrophenethyl alcohols were prepared by reduction of the corresponding acids with sodium borohydride in the presence of aluminium trichloride (a method specific for the reduction of CO_2H to $CH_2{\cdot}OH$ in the presence of nitro-groups [13]) and were converted into the methyl ethers with diazomethane.[14]

Methyl phenethyl ether was nitrated with nitric acid alone, with mixed acid, with nitric acid in acetic anhydride (the system most commonly used for studying the reactions of acetyl nitrate), and with acetyl nitrate in acetonitrile. The temperature of reaction was constant within $\pm 0{\cdot}5°$, and in all reactions less than one equivalent of nitrating agent was used in order to minimise dinitration. The mixtures of nitro-derivatives were analysed by gas chromatography, complete resolution of the three isomers being obtained. Isomer distributions are set out in Table 1.

TABLE 1. *Nitration of methyl phenethyl ether.*

		Orientation (%)		
Nitrating agent	Temp.	*ortho*	*meta*	*para*
Nitric–sulphuric acid	0°	28·9	8·7	62·4
	25	31·6	9·4	59·0
Nitric acid	25	40·2	6·6	53·2
Nitric acid in nitromethane	25	41·2	3·0	55·8
Nitric acid in acetic anhydride	0	64·4	3·6	32·0
	25	62·3	3·7	34·0
Acetyl nitrate in acetonitrile	0	66·0	4·2	29·8

We found that, as occurred with anisole and acetanilide, the *ortho* : *para*-ratio is considerably higher in nitrations by acetyl nitrate. The *meta* : *para*-ratios, however, are essentially the same for nitration with nitric acid and with acetyl nitrate. If the change in orientation were the result of protonation of the oxygen atom in the aromatic compound by nitric acid, not only would the *ortho* : *para*-ratio be lower in the acid conditions, but the *meta* : *para*-ratio should be higher, for such protonation would result in greater deactivation of the *para*- than of the *meta*-position. This is not the case, although the slightly greater

[11] Roberts, Sanford, Sixma, Cerfontain, and Zagt, *J. Amer. Chem. Soc.*, 1954, **76**, 4525.
[12] Bird and Ingold, *J.*, 1938, 918.
[13] Brown and Subba Rao, *J. Amer. Chem. Soc.*, 1956, **78**, 2582.
[14] Müller and Rundel, *Angew. Chem.*, 1958, **70**, 105.

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proportion of *m*-nitro-derivative with mixed acid is compatible with a small degree of protonation. Nor can the change be due to the fact that nitration with nitric acid takes place in a two-phase system while that with acetyl nitrate takes place in homogeneous conditions, for nitration with nitric acid in nitromethane solution gives essentially the same *ortho* : *para*-ratio as nitric acid alone. Because the degree of nitration by nitric acid in nitromethane was extremely small, even after very long reaction times, the results under these conditions are not considered as accurate as the remainder.

Thus the variation in *ortho* : *para*-ratios results not simply from a diminished reactivity of the *ortho*-position in acid solutions. (Further evidence for this conclusion is adduced later.)

That toluene gives *o*- and *p*-nitro-derivatives in the same proportions with acetyl nitrate as with nitric acid [6] is evidence that there is a nitrating species common to both systems. This must be the nitronium ion, which is known to be responsible for nitration with nitric acid. Yet if the nitronium ion alone were responsible for nitration of the ether with acetyl nitrate, the isomer ratio should be the same as that for nitration with nitric acid. There must therefore be another nitrating species present in acetyl nitrate which is capable of nitrating only the *ortho*-position of the ether, and not either the *para*-position of the ether or the *ortho*- or *para*-position of toluene. This conclusion is supported by a comparison of the partial rate factors for the nitration by acetyl nitrate of methyl phenethyl ether with those of ethylbenzene.[15] The former compound is very much less reactive

TABLE 2. *Rate factors for nitration.*

Compound	*ortho*	*meta*	*para*
$Ph{\cdot}CH_2{\cdot}CH_2{\cdot}OMe$	25·9	1·5	25·8
$Ph{\cdot}CH_2{\cdot}CH_3$	31·4	2·3	69·5

than the latter in the *para*-position, consistently with the electron-withdrawing nature of the methoxyl group, but the two hardly differ in reactivity at their *ortho*-positions, suggesting that an additional mode of nitration at the *ortho*-position of the ether approximately counterbalances the loss in reactivity expected to result from substitution of methoxyl for hydrogen.

Nitration of methyl phenethyl ether with benzoyl nitrate and with *p*-nitrobenzoyl nitrate in acetonitrile solution gives nitro-derivatives in the same proportions as when acetyl nitrate is the reagent ($BzNO_3$ and $NO_2{\cdot}C_6H_4{\cdot}CO{\cdot}NO_3$ respectively: *ortho* 65·7, 64·9; *meta* 3·6, 4·7; *para* 30·7, 30·4%). We conclude from this that the species which is responsible for the enhanced *ortho*-reactivity is common to these three acyl nitrates. The only nitrating species (other than NO_2^+) known to be present in such systems is dinitrogen pentoxide.[16] There is evidence that the nitration by benzoyl nitrate of comparatively unreactive aromatic compounds (such as chlorobenzene) involves dinitrogen pentoxide as the active species,[17] although Paul found that the kinetics of the nitration of benzene with nitric acid in acetic anhydride were compatible with attack by the nitronium ion but not with attack by dinitrogen pentoxide.[18] That dinitrogen pentoxide is the reagent responsible for the high proportion of *ortho*-substitution in the present case is supported by our finding that dinitrogen pentoxide itself gives rise to the same isomer distribution as the acyl nitrates (see Table 3). Further, toluene gives the same isomer distribution with dinitrogen pentoxide as with acetyl nitrate.

Our results, together with the other evidence which we have discussed, are compatible with the following mechanism for the enhanced reactivity of the *ortho*-position of methyl phenethyl ether in its reaction with acyl nitrates. The acyl nitrate, itself not reactive

[15] Knowles, Norman, and Radda, *J.*, 1960, 4885.
[16] Chèdin and Fénéant, *Compt. rend.*, 1949, **229**, 115; Malkova, *J. Gen. Chem.* (*U.S.S.R.*), 1954, **24**, 1151; Vandoni and Viala, *Mem. Services chim. État*, 1945, **32**, 80.
[17] Gold, Hughes, and Ingold, *J.*, 1950, 2467.
[18] Paul, *J. Amer. Chem. Soc.*, 1958, **80**, 5329.

enough to bring about nitration of the aromatic compound, gives rise to dinitrogen pentoxide (and acyl anhydride) which reacts in two ways. It undergoes slow heterolysis to the nitronium ion which reacts with the aromatic compound to give *o*-, *m*-, and *p*-nitro-derivatives in the same proportions as when nitric acid is the reagent; and at the same time

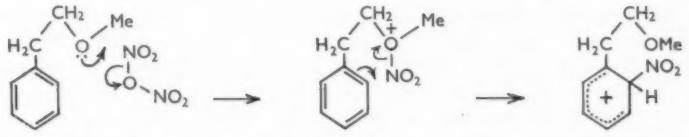
TABLE 3. *Orientation* (%) *of nitration by dinitrogen pentoxide in acetonitrile at* 0°.

Compound	*ortho*	*meta*	*para*
Methyl phenethyl ether	68·8	3·3	27·9
Toluene	59·8	3·3	36·9

there is an additional mode of nitration at the *ortho*-position, dependent on the presence of the oxygen atom of the ether, and brought about by dinitrogen pentoxide itself.

It is possible that nitronium ion might be generated directly from the acyl nitrate by heterolysis of the O–N bond. If this were to happen, it is unlikely that each of three acyl nitrates should generate nitronium ion and dinitrogen pentoxide at the same relative rates, as is required by the finding that the isomer distribution is constant for these three reagents. This route to nitronium ion can probably be excluded.

The rôle of the oxygen atom of methyl phenethyl ether has now to be explained. We consider that nitration by dinitrogen pentoxide involves an S_N2-type displacement (as shown) in which the oxygen atom displaces nitrate ion from covalent dinitrogen pentoxide, giving a charged intermediate. This rearranges through a six-membered cyclic transition state to the usual σ-bonded intermediate of aromatic nitration and thence to the *o*-nitro-derivative. This provides a route for the formation of the *o*-nitro-derivative which is



available neither at the *para*-position of the ether, nor at the *ortho*-positions of ethylbenzene or toluene. It is reasonable that the displacement occurs on dinitrogen pentoxide rather than on the acyl nitrate as our observations require, because the nitrate ion has greater stability than a carboxylate ion and should therefore be a better leaving group in such displacements. It is known also that the *O*-nitration of alcohols by acetyl nitrate involves dinitrogen pentoxide as the attacking entity.[19]

The following evidence supports the cyclic mechanism proposed above:

(i) Addition of a catalytic amount of sulphuric acid in the nitration of methyl phenethyl ether with acetyl nitrate decreases the proportion of *o*-nitro-derivative from 62·3 to 55·1%, while the *meta* : *para*-ratio remains effectively constant. The orientation, at 25°, is: $o : m : p = 55{\cdot}1 : 5{\cdot}0 : 39{\cdot}9$. The constancy of the *meta* : *para*-ratio argues against prescription of the fall in the proportion of *ortho*-isomer to protonation of the ether. On the other hand, there is evidence that both nitric and sulphuric acid bring about the dissociation of dinitrogen pentoxide into nitronium ions, the kinetic results for the reaction with nitric acid having been interpreted on the basis that the acid molecules aggregate around the pentoxide causing ionic dissociation:[20] $NO_2{\cdot}O{\cdot}NO_2 + (x + y)HNO_3 \rightleftharpoons NO_2^+(xHNO_3) + NO_3^-(yHNO_3)$. This increases the rate of " normal " nitration relatively to that which occurs by displacement on dinitrogen pentoxide.

(ii) The operation of a mechanism similar to that proposed for methyl phenethyl ether in the case of methyl 3-phenylpropyl ether would involve the formation of a seven-membered cyclic transition state which should be less readily formed than its six-membered analogue. We found that the nitro-derivatives of methyl 3-phenylpropyl ether are

[19] Bonner, *J.*, 1959, 3908.
[20] Gold, Hughes, Ingold, and Williams, *J.*, 1950, 2452.

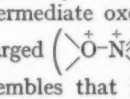
formed (at 0°) in essentially the same proportions when nitric acid (*o* 44·2, *m* 3·8, *p* 52·0%) or acetyl nitrate (*o* 43·0, *m* 4·0, *p* 53·0%) is the reagent.

(iii) Benzyl methyl ether gives rise to a higher proportion of its *o*-nitro-derivative with acetyl nitrate than with nitric acid (see Table 4). A mechanism analogous to that proposed for nitration of methyl phenethyl ether would involve formation of a five-membered cyclic transition state, which should be easy. (The first two results in Table 4 are not as accurately established as those for nitration of methyl phenethyl ether because the extent of nitration was kept extremely small in order to avoid side-reactions.)

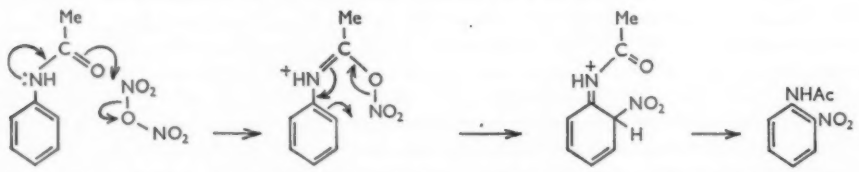
TABLE 4. *Orientation* (%) *of nitration of benzyl methyl ether at* 25°.

Nitrating agent	*ortho*	*meta*	*para*
Nitric acid	38·5	12·8	48·7
Nitric acid–sulphuric acid [21]	28·6	18·1	53·3
Nitric acid in acetic anhydride [21]	51·3	6·8	41·9

Finally, comparison of the partial rate factors for the nitration by acetyl nitrate of methyl phenethyl ether with those of methyl 3-phenylpropyl ether (*o* 14·6, *m* 1·2, *p* 34·3) further supports the conclusion that the variation in the *ortho* : *para*-ratios does not result from diminished reactivity of the *ortho*-position in acid solutions. The greater reactivity of the *para*-position in the 3-phenylpropyl ether than in the phenethyl ether results from the greater distance of the methoxyl group from the aromatic ring in the former compound. The greater reactivity of the *ortho*-position in the phenethyl ether than in the phenylpropyl ether indicates that there is an enhancement of the reactivity of the *ortho*-position in the first compound.

In summary, all the facts are satisfactorily correlated by the proposal that, in acyl nitrate systems, methyl phenethyl ether is nitrated at the *ortho*-position not only by the nitronium ion but also by the sterically favourable rearrangement of an oxonium ion formed by reaction of dinitrogen pentoxide with the oxygen of the ether. That this intermediate oxonium ion has two atoms bonded together each of which is positively charged  is compatible with the existence of the ion as an intermediate, for it resembles that involved in the nitramine rearrangement.[22] The mechanism also has certain features in common with that accepted for the Claisen rearrangement;[23] and it is notable that methyl phenethyl sulphide gives an unusually high proportion of *ortho*-derivative in a Friedel–Crafts reaction.[24]

It is tempting to extend the mechanism proposed above to include the reactions of anisole and acetanilide. Thus, the mechanism for the increased *ortho*-reactivity in the nitration of acetanilide with acetyl nitrate would be as follows:



We have found that anisole gives the same proportions of nitro-derivatives with dinitrogen pentoxide (at 0°: *o* 70·9, *m* 0, *p* 29·1%) as with acetyl nitrate (*o* 70·0, *m* 0, *p* 30·0%), which accords with Halvarson and Melander's proposal [6] that in this reaction the oxygen atom of anisole may react with dinitrogen pentoxide to form an intermediate which rearranges to the *o*-nitro-derivative. We consider that this process may be represented analogously,

[21] Knowles and Norman, *J.*, 1961, 2938.
[22] Brownstein, Bunton, and Hughes, *J.*, 1958, 4354.
[23] Ref. 1, p. 598.
[24] Saunders and Edison, *J. Amer. Chem. Soc.*, 1960, **82**, 138.

though confirmation of such reaction paths for anisole and acetanilide awaits further experimentation.

Experimental

Materials.—Fuming nitric acid (B.D.H. " AnalaR; " *d* 1·5) was used in all quantitative nitrations. Acetic anhydride, acetyl chloride, benzoyl chloride, *p*-nitrobenzoyl chloride, acetonitrile, nitromethane, toluene, anisole, and benzyl methyl ether were commercial materials purified by distillation. Methyl phenethyl ether was prepared by Gupta, Lal, and Shukla's method [25] and purified by three fractional distillations, the final product being collected at 192—193°. Methyl 3-phenylpropyl ether was prepared similarly, from 3-phenylpropan-1-ol (101 g.), dimethyl sulphate (70 ml.), and sodium hydroxide (59 g.). The product was purified by fractional distillation, the fraction boiling at 213° (66 g., 59%) being collected.

Syntheses of Reference Compounds.—The nitro-derivatives of anisole were commercial materials which were purified by recrystallisation or distillation, their purities being checked by gas chromatography. The nitro-derivatives of toluene and benzyl methyl ether were available.[15,21]

Methyl 4-nitrophenethyl ether. 4-Nitrophenethyl bromide [26] (5·1 g.) in hot methanol (10 ml.) was added to a solution of sodium (1·5 g.) in methanol (10 ml.), and the mixture was refluxed for 2 hr. After cooling, water was added and organic material was extracted with ether and washed with water. Evaporation gave pale yellow *methyl 4-nitrophenethyl ether*, m. p. 62·5—63° (from light petroleum) (Found: C, 59·7; H, 6·6; N, 7·6. $C_9H_{11}NO_3$ requires C, 59·7; H, 6·1; N, 7·7%).

Methyl 2-nitrophenethyl ether. *o*-Nitrophenylacetic acid [27] (6 g., 0·03 mole) and sodium borohydride (3 g., 0·09 mole) were dissolved in diethylene glycol dimethyl ether (dried over lithium hydride and distilled under reduced pressure) (62 ml.). Aluminium trichloride (purified by sublimation) (1 g.) in diethylene glycol dimethyl ether (8 ml.) was slowly added to this solution. The mixture was kept at 50—60° for 3 hr. After decomposition of the excess of sodium borohydride with ice and dilute hydrochloric acid, the ether extract was dried (Na_2SO_4) and the solvents were removed. Distillation yielded 2-nitrophenethyl alcohol, b. p. 133°/0·3 mm. (lit.,[28] 155°/1 mm.) (5·1 g., 92%). This reduction when carried out on a larger quantity of the acid (22 g.) gave only a 60% yield. Diazomethane, from " Diazald " (21·9 g.), was distilled, with ether, into an ice-cooled solution of 2-nitrophenethyl alcohol (5·9 g.) and the boron trifluoride–ether complex (0·6 g.) in dry ether. After 3 hr. at room temperature the solution was washed with water. *Methyl 2-nitrophenethyl ether* was purified by chromatography on alumina in light petroleum–benzene (1 : 1 v/v) to give a pale yellow liquid, n^{25} 1·5274 (2·3 g., 36%) (Found: C, 60·7; H, 6·3; N, 7·8%).

Methyl 3-nitrophenethyl ether. *m*-Nitrophenylacetic acid [29] (18 g.) was reduced as described for the *o*-nitro-compound, and gave yellow needles of *3-nitrophenethyl alcohol* (11 g., 69%), m. p. 48·5—49·5° (from light petroleum–benzene) (Found: C, 57·4; H, 5·4; N, 8·6. $C_8H_9NO_3$ requires C, 57·5; H, 5·4; N, 8·4%). The alcohol was methylated as described for the *o*-nitro-compound, giving the *ether* (30%), m. p. 28—28·5° (from light petroleum–benzene) (Found: C, 59·5; H, 6·2; N, 7·8%).

Nitro-derivatives of methyl 3-phenylpropyl ether. These compounds were not characterised separately. When log (retention time) was plotted against the number of carbon atoms in the mononitro-derivatives of benzyl methyl ether, methyl phenethyl ether, and methyl 3-phenylpropyl ether (the nitro-derivatives of the last compound being obtained as a mixture by direct nitration), three straight lines were obtained. Each passed through three points, two of which corresponded to nitro-derivatives of the first two compounds having the same orientation, while the third corresponded to one nitro-derivative of methyl 3-phenylpropyl ether. Since the logarithm of the retention time of each member of a homologous series, measured under the same conditions, is proportional to the number of carbon atoms in the chain,[30] it was concluded

[25] Gupta, Lal, and Shukla, *J. Proc. Inst. Chemists (India)*, 1956, **28**, 39. (*Chem. Abs.*, 1956, **50**, 14,178.)
[26] Foreman and McElvain, *J. Amer. Chem. Soc.*, 1940, **62**, 1435.
[27] Reissert, *Ber.*, 1897, **30**, 1041; 1908, **41**, 3814, 3925.
[28] Sebastien, Sabetay, and Blèger, *Bull. Soc. chim. France*, 1931, **49**, 3.
[29] Gabriel and Borgman, *Ber.*, 1883, **16**, 2064.
[30] Ray, *J. Appl. Chem.*, 1954, **4**, 21; James and Martin, *Biochem. J.*, 1952, **50**, 679.

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that the order of retention times of the nitro-derivatives of methyl 3-phenylpropyl ether was *o*- < *m*- < *p*- (see Table 5).

TABLE 5. *Retention times of nitro-derivatives.*

Compound	Retention times of derivatives (min.) 2-Nitro	3-Nitro	4-Nitro
Benzyl methyl ether	26·8	34·8	39·0
Methyl phenethyl ether	40·0	55·0	62·0
Methyl 3-phenylpropyl ether	57·0	80·0	94·0

Nitrations.—Reactions were carried out at 0° and 25°, the nitrating mixture (0·005 mole) being added to the aromatic compound (0·01 mole) during 1 hr. with shaking. The temperature variation was not more than 0·5°. Individual nitration mixtures and reaction times were as follows:

Nitric acid in acetic anhydride. A solution of nitric acid (0·005 mole) in acetic anhydride (0·005 mole) was made up at 0°. Nitration of the aromatic compound was stopped after 2 hr. by addition of water.

Nitric–sulphuric acid. A 1 : 1 (v/v) mixture of the two acids was used. Reaction with the aromatic compound was continued for 2 hr. after addition of all the nitrating mixture.

Nitric acid. A longer time (5 hr.) was necessary to obtain a sufficient degree of nitration for accurate analysis.

Nitric acid in nitromethane. The aromatic compound (0·01 mole) was dissolved in nitromethane (0·5 ml.), and nitric acid (0·005 mole) was added in the usual manner. The extent of nitration was small even after 40 hr.

Acyl nitrates in acetonitrile. The acyl nitrate was prepared *in situ*.[31] Silver nitrate (0·005 mole) and the aromatic compound (0·01 mole) were dissolved in acetonitrile (1 ml.), and a solution of the acyl chloride (0·005 mole) in acetonitrile (0·4 ml.) was added slowly at the required temperature. Reaction was stopped after 3 hr.

Dinitrogen pentoxide in acetonitrile. Dinitrogen pentoxide [20] (0·005 mole) was dissolved in acetonitrile (0·4 ml.), and the solution was added slowly to the aromatic compound (0·01 mole) in acetonitrile (1 ml.). The reaction time was 3 hr.

Gas Chromatography.—After nitration had been stopped by the addition of water, the reaction mixtures were extracted with ether four times and the ethereal solutions, after being concentrated, were analysed by gas chromatography. The optimum conditions found for analysis of the nitro-derivatives of the aromatic substrates are set out in Table 6. The column was packed with Apiezon " L " grease (20% w/w) coated on Embacel except for the resolution of the nitroanisoles, for which it was packed with 2,4,7-trinitrofluorenone (10% w/w) coated on firebrick.[32] The carrier-gas was nitrogen; a hydrogen-inject flame ionisation detector coupled to a Sunvic recorder gave a linear response.

TABLE 6. *Operating conditions and retention times for analysis of nitro-derivatives.*

Aromatic compound	Column length (cm.)	Flow-rate (ml./min.)	Temp.	Retention times (min.) *o*	*m*	*p*
Methyl phenethyl ether	200	25	175°	36	50	60
Methyl 3-phenylpropyl ether	400	30	185	57	80	94
Benzyl methyl ether	200	30	160	30	43	52
Anisole	200	20	175	60	72	80

In the conditions set out, the three nitro-isomers of each compound were completely resolved. The isomer distributions were calculted by measuring the peak areas as described previously.[15] It was shown by injecting synthetic mixtures that the peak areas were proportional to the amounts of the isomers present. It was also shown, by subjecting synthetic mixtures of isomers to the same extraction procedure as that used for the reaction mixtures, that no preferential loss of any of the isomers occurred. The results reported are in every case the mean values from the analyses of at least two nitrations each of which was analysed at least twice. Some representative analyses are set out in Table 7.

[31] Burton and Praill, *J.*, 1955, 729.
[32] Norman, *Proc. Chem. Soc.*, 1958, 151.

TABLE 7. *Analysis of some nitration mixtures.*

Compound	Nitrating agent	Temperature	Isomer distribution *ortho*	*meta*	*para*
$Ph{\cdot}CH_2{\cdot}CH_2{\cdot}OMe$	HNO_3	25°	40·1, 40·4, 40·2	7·0, 6·2, 6·8	52·9, 53·7, 52·8
$Ph{\cdot}[CH_2]_3{\cdot}OMe$	HNO_3–Ac_2O	0	44·7, 43·7	4·0, 3·6	51·3, 52·7

The conditions used for analysis of the nitrotoluenes were as those reported previously.[15]

Competitive Nitrations.—The overall reactivities of methyl phenethyl and 3-phenylpropyl ether relatively to that of toluene were determined, for nitration by acetyl nitrate at 0°, by the method reported previously.[15] Decane was used as the internal standard. Using the value of 27 for the reactivity of toluene relative to benzene, measured under the same conditions as ours,[33] enabled the overall reactivities relative to that of benzene to be calculated. These are shown in Table 8.

TABLE 8. *Competitive experiments.*

Compound	Reactivity rel. to toluene	Rel. to C_6H_6
$Ph{\cdot}CH_2{\cdot}CH_2{\cdot}OMe$	0·445, 0·493, 0·585, 0·445, 0·548, 0·445	—
	average 0·493 ± 0·050	13·4 ± 1·3
$Ph{\cdot}[CH_2]_3{\cdot}OMe$	0·378, 0·441, 0·374, 0·434, 0·378	—
	average 0·401 ± 0·029	10·8 ± 0·8

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, December 29th*, 1960.]

[33] Ingold, Lapworth, Rothstein, and Ward, *J.*, 1931, 1959.

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581. *The Reactions of Methyl and Ethyl Radicals with Hydrogen Bromide and the Strength of* C–H *Bonds.*

By G. C. FETTIS and A. F. TROTMAN-DICKENSON.

Acetone and ethyl methyl ketone have been photolysed in the presence of hydrogen bromide and iodine. The relative rates of attack by the alkyl radicals on the additives have been found, and the activation energies and heats of reactions calculated. Thence it is found that D(Me–H) = 103·9 and D(Et–H) = 98·2 kcal. mole^{-1} at 25°, and it is suggested that D(Pr^i–H) = 94·5 and D(Bu^t–H) = 91·4 kcal. mole^{-1}.

THE accepted value, 102·5 kcal. mole^{-1} at 25°, of the dissociation energy of the C–H bond in methane is based on studies of bromination and electron impact,[1] agreement between results of the two methods being good. Consequently $D(CH_3{-}H)$ is often regarded as known to a greater accuracy than could be claimed for either of the methods alone. Determination of the bond strength by bromination is based on the equation:

$$D(CH_3{-}H) = D(H{-}Br) + E_1 - E_{-1}$$

where E_1 is the activation energy of the forward and E_{-1} of the back-reaction:

$$Br + CH_4 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} HBr + CH_3\cdot \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

E_1 is accurately known; E_{-1} is less certain. Two attempts [2,3] have been made to relate E_{-1} to E_2 which is the activation energy of the reaction:

$$CH_3\cdot + I_2 \longrightarrow CH_3I + I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

It is widely accepted that this reaction has no activation energy, so that $E_{-1} - E_2 = E_{-1}$. Both attempts depended on the photolysis of methyl iodide as the source of radicals.

[1] Cottrell, "The Strengths of Chemical Bonds," Butterworths, London, 1960.
[2] Andersen and Kistiakowsky, *J. Chem. Phys.*, 1943, **11**, 6.
[3] Williams and Ogg, *J. Chem. Phys.*, 1947, **15**, 696.

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Consequently the products of reaction (2) could not be determined directly: they had to be inferred from observation of the dependence of the yield of methane on the concentrations of hydrogen bromide and iodine.

The advent of gas chromatography has simplified the determination of methyl iodide in the presence of material of similar boiling point. k_{-1}/k_2 can now be found from the relation:

$$\frac{k_{-1}}{k_2} = \frac{\mathrm{d}[CH_4]/\mathrm{d}t \,.\, [I_2]}{\mathrm{d}[CH_3I]/\mathrm{d}t \,.\, [HBr]},$$

when the radicals are formed by the photolysis of acetone in the presence of hydrogen bromine and iodine. If only a small proportion of the reagents is consumed, then

$$\frac{k_{-1}}{k_2} = \frac{(CH_4)}{(CH_3I)} \cdot \frac{[I_2]}{[HBr]},$$

where the first term is the ratio of the total amounts of methane and of methyl iodide formed.

Much less is known about ethyl radicals. E_1^* for the attack of a bromine atom on ethane has only recently been reliably measured.[4,5] No measurement of E_{-1}^* has been reported. However, a relation analogous to that above may be derived for ethyl radicals produced by photolysis of ethyl methyl ketone.

Experimental

Apparatus.—The quartz reaction vessel (600 c.c.) was attached to a conventional high-vacuum apparatus. It was contained in an electric furnace into which light from a 125 w mercury arc was focused by a quartz lens. Part of the connecting tubing was wound with heating ribbon to prevent condensation of iodine vapour. Stopcocks were lubricated with silicone grease.

Materials.—Reagent-grade iodine was sublimed twice over potassium iodide and thoroughly degassed. Acetone and ethyl methyl ketone were commercial samples. Hydrogen bromide was prepared by the action of bromine on tetralin, catalysed by powdered aluminium.

Procedure.—Iodine was introduced into the reaction vessel to a pressure determined by the temperature of the water-bath surrounding the storage vessel. Ketone, followed by hydrogen bromide, was measured on a mercury manometer. At the end of the reaction the contents of the cell were distilled through an absorption tube into the chromatography trap. With ethyl methyl ketone, the tube was packed with 3″ of potassium thiosulphate crystals, 2″ of 30% calcium carbonate–ethylene glycol on firebrick (25—52 mesh), and 1″ of magnesium perchlorate to remove iodine, hydrogen bromide, and water. With acetone, the iodine was removed by 40% sodium thiosulphate–firebrick (40—60 mesh) (heated to coat the firebrick), and the hydrogen bromide was adsorbed by an alumina column which was frequently changed.

The products of the ethyl radical reactions were separated on split columns of 3′ Celite (80—100 mesh) + 20% of diethyl phthalate (35°) and 2½′ alumina (40—60 mesh) at 0°. The products of methyl radical reactions were separated on 6½′ Celite (40—60 mesh) +18% of diethyl phthalate at 30° and 3′ of activated charcoal (60—80 mesh) at room temperature. When the charcoal column was by-passed, the gas flowed through a column of glass beads of equal resistance. The carrier gas was hydrogen. The detector was a thermal conductivity cell.

Results and Discussion

The results for methyl and ethyl radicals are given in Tables 1 and 2. Least-squares treatment yields, for methyl radicals:

$$\log (k_{-1}/k_2) = (-0{\cdot}300 \pm 0{\cdot}131) - (1370 \pm 261/2{\cdot}3RT),$$

and for ethyl radicals:

$$\log (k_{-1}^*/k_2^*) = (0{\cdot}228 \pm 0{\cdot}036) - (2{\cdot}288 \pm 80/2{\cdot}3RT).$$

[4] Fettis and Trotman-Dickenson, *J. Amer. Chem. Soc.*, 1959, **81**, 5260.
[5] Fettis, Knox, and Trotman-Dickenson, *J.*, 1960, 4177.

Vol. 1961, page 3039, line 25. *For* 103·9 kcal. mole^{-1} *read* 86·5 kcal. mole^{-1}; and line 26, *for* 98·2 kcal. mole^{-1} *read* 103·9 kcal. mole^{-1}.

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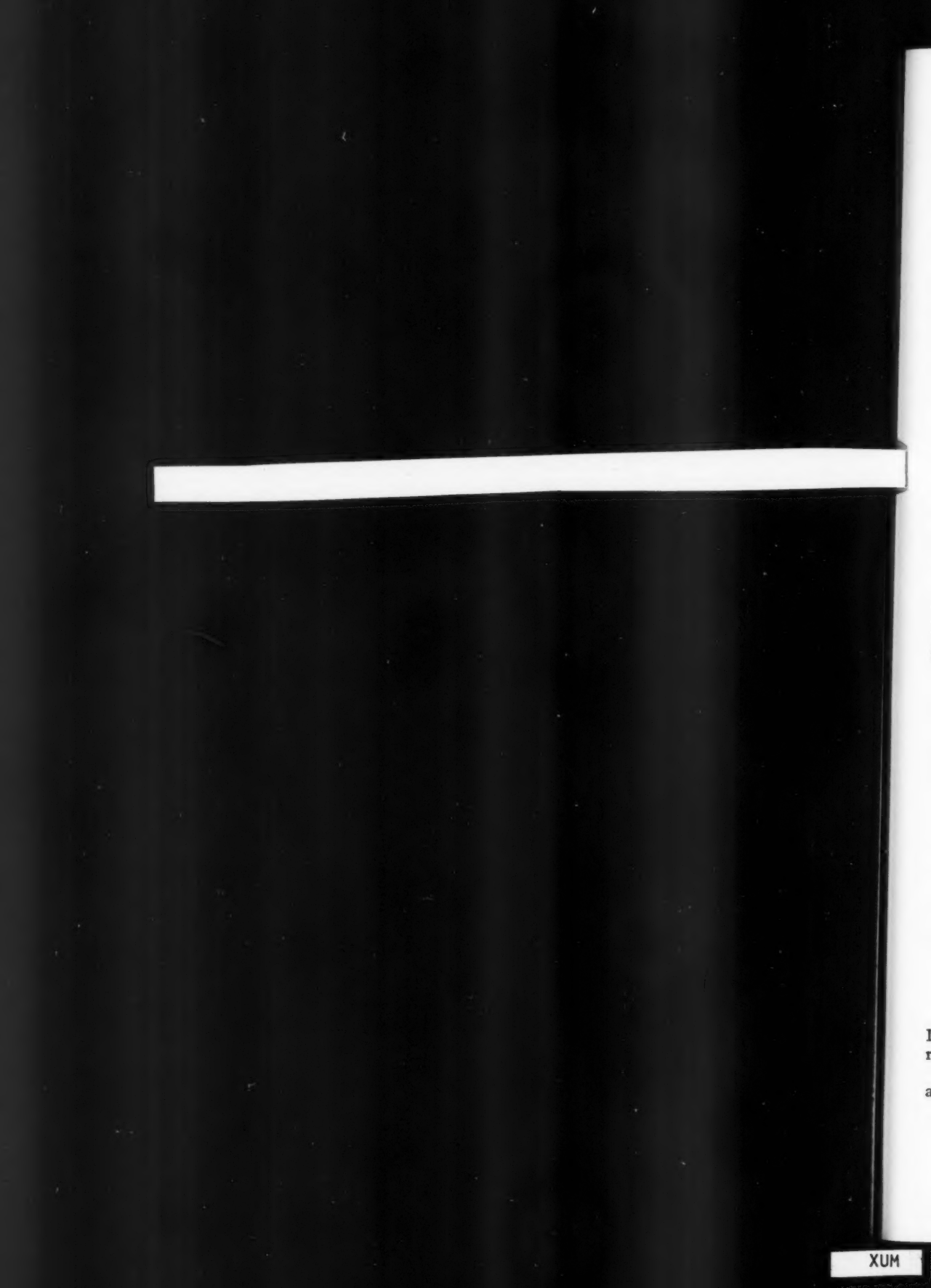

The extrapolated value for k_{-1}/k_2 at 60° is 0·063, in excellent agreement with the mean value 0·055 found by Andersen and Kistiakowsky.[2] The agreement with Williams and Ogg's value,[3] 0·042, at 140° is less good (0·095).

TABLE 1. *The reactions of methyl radicals with iodine and hydrogen bromide.*

Temp.	I_2 (mm.)	HBr (cm.)	Me_2CO (cm.)	$\frac{k(MeI)}{k(MeH)}$	Temp.	I_2 (mm.)	HBr (cm.)	Me_2CO (cm.)	$\frac{k(MeI)}{k(MeH)}$
80°	4·57	3·95	4·90	23·48	164°	4·57	6·02	5·00	18·75
80	,,	4·07	4·75	23·44	164	,,	4·60	5·38	16·14
80	,,	4·40	5·25	24·95	164	,,	7·37	6·48	14·68
112	,,	4·40	4·88	18·11	164	,,	4·70	3·30	18·32
112	,,	5·46	7·04	19·17	244	,,	5·10	4·88	12·64
112	,,	4·40	4·80	16·39	244	,,	4·95	4·90	12·67
112	2·24	4·74	4·10	19·80	244	,,	3·65	5·40	15·10
164	4·57	4·55	4·80	18·45	244	,,	2·15	6·50	12·05
164	,,	4·45	5·05	15·08	288	,,	5·10	5·30	10·00
164	,,	5·28	4·90	17·05	288	,,	4·70	5·30	10·00
164	,,	5·83	3·94	13·41	288	,,	4·40	6·40	10·78
164	,,	4·98	5·91	16·57	288	8·61	3·60	3·18	11·81

* Pyrex filter used.

Fettis, Knox, and Trotman-Dickenson [5] found that E_1 for methane is 18·25 kcal. mole^{-1} and E_1* for ethane is 13·40 kcal. mole.$^{-1}$.

The mean temperature of the methane reactions was sufficiently close to 460° K for both the forward and the reverse reaction for us to be able to write:

$$D(CH_3\text{–}H)^{460} = D(H\text{–}Br)^{460} + E_1 - E_{-1} = 87{\cdot}9 + 16{\cdot}95 = 104{\cdot}85 \text{ kcal. mole}^{-1}.$$

$D(H\text{–}Br)^{460}$ is obtained from the value of 103·9 kcal. mole^{-1} at 0° K.

Hence $D(CH_3\text{–}H)^{298} = 98{\cdot}2$ kcal. mole^{-1}.

Similarly $D(C_2H_5\text{–}H)^{298} = 98{\cdot}2$ kcal. mole^{-1}.

TABLE 2. *The reactions of ethyl radicals with iodine and hydrogen bromide.*

Temp.	I_2 (mm.)	HBr (cm.)	COEtMe (cm.)	$\frac{k(EtI)}{k(EtH)}$	Temp.	I_2 (mm.)	HBr (cm.)	COEtMe (cm.)	$\frac{k(EtI)}{k(EtH)}$
54·5°	2·24	4·20	4·95	39·93	119·2°	4·57	4·48	4·36	23·66
59·0	3·24	4·67	4·85	36·93	,,*	,,	4·75	5·05	21·99
65·0	4·57	4·54	4·31	32·28	143·0	,,	5·00	5·73	15·85
72·5	,,	4·34	4·60	35·14	,,	,,	4·26	6·42	15·55
73·5	,,	3·63	4·55	31·77	,,	,,	6·10	5·48	19·14
,,	,,	3·01	4·72	28·70	,,	,,	3·02	5·64	16·07
74·5	,,	3·60	4·85	31·11	,,	,,	2·23	6·95	17·54
88·0	,,	4·79	5·15	26·47	,,	2·24	4·94	5·65	17·87
,,	,,	3·58	6·62	26·98	173·5	4·57	5·80	7·25	14·26
87·5	,,	4·28	4·26	24·97	175·0	8·61	5·85	7·85	14·06
,,	,,	4·74	4·42	30·15	,,	4·57	5·11	6·18	14·35
89·0	,,	5·56	3·87	27·05	,,	8·61	6·38	7·85	11·61
,,	,,	6·03	3·15	28·27	,,	4·57	4·50	6·95	15·40
,,	,,	3·29	3·30	26·83	,,	8·61	4·78	7·35	11·40
101·5	,,	3·81	4·57	25·24	179·0	4·57	4·04	6·48	15·98
,,	,,	3·70	4·67	24·71	,,	,,	5·46	6·72	16·37
114·5	,,	4·45	4·82	20·93	,,	,,	5·96	7·49	16·44
,,	,,	4·90	5·45	22·91					
,,	,,	4·76	2·84	22·80					
,,	,,	4·70	4·25	22·35					

* Pyrex filter used.

In both instances it was assumed that the heat capacities of the hydrocarbon and its radical were identical.

The difference between the above value and that found for $D(CH_3\text{–}H)$ by Kistiakowsky and Van Artsdalen [6] arises mainly from three causes. The first, which is independent

[6] Kistiakowsky and Van Artsdalen, *J. Chem. Phys.*, 1944, **12**, 469.

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of kinetic work, is that a higher value for D(H–Br) has been adopted: the higher value has been universally accepted in recent years. The second reason is that 18·25 kcal. mole^{-1} rather than 17·8 kcal. mole^{-1} has been taken for E_1. The difference arises because we have adopted the simple Arrhenius definition of the activation energy, whereas Kistiakowsky and Van Artsdalen used a " collision theory " activation energy derived from the equation, $k = BT^{\frac{1}{2}} \exp(-H/\boldsymbol{R}T)$. The Arrhenius equation is known to be inadequate, but so also is the collision form. It seems best to use the simpler equation in this case. Unfortunately the errors consequently introduced into E_1 and E_{-1} do not cancel because E_{-1} is not found absolutely but only in terms of E_2. The third and most direct reason is that we have measured $E_{-1} - E_2$ and found it to be 0·7 kcal. mole less than the value of E_{-1} assumed by Kistiakowsky and Van Artsdalen.[6]

The probable errors in the present determination of the bond strengths are of three kinds. First are those that can be evaluated statistically, arising from the limitations of our measurements. For ethane they are very small: $E_1^* = 13{\cdot}40 \pm 0{\cdot}09$ and $E_{-1}^* - E_2^* = 2{\cdot}29 \pm 0{\cdot}08$; for methane, $E_{-1} - E_2 = 1{\cdot}3 \pm 0{\cdot}3$. The error in E_1 cannot be readily found but the independent determination by Kistiakowsky and Van Artsdalen is in complete agreement with that given here. The second kind of error arises because both E_1 and E_1^* are ultimately based on Kistiakowsky and Van Artsdalen's activation energy for the attack of bromine atoms on methyl bromide. It should be noted that this uncertainty does not affect the determination of $D(CH_3\text{–H}) - D(C_2H_5\text{–H})$. The third kind of error arises from the uncertainty of the activation energies for the attack of radicals on iodine. We have accepted the view that it is zero. The best evidence for this value is Christie's work [7] on the comparison of the rates of reaction of methyl radicals with oxygen and iodine. She found that at room temperature $k_2 = 10^{13}$ mole^{-1} c.c. sec.$^{-1}$ and remarked that this value is consistent with a steric factor of unity and a low activation energy. Rough calculations on the basis of the theory of absolute reaction rates, which has been successful in predicting the A factors of alkane–halogen reactions,[8] indicate that A_2 should lie between $10^{11{\cdot}5}$ and $10^{12{\cdot}5}$ mole^{-1} c.c. sec.$^{-1}$. Accordingly the evidence in favour of $E_2 = 0$ is better than Christie suggests. If E_2 is greater than this, then the calculated bond strengths are too high. It seems reasonable to attach errors of ± 1 kcal. mole^{-1} to the bond strengths found here and smaller errors, say 0·3 kcal. mole^{-1}, to the important bond-strength differences. The overall error is close to that usually quoted, but the values are likely to be more reliable.

Although this work provides direct evidence on the strengths of only methyl and ethyl bonds some conclusions can be drawn about the C–H bonds formed by other alkyl radicals. Fettis and Trotman-Dickenson [4] deduced values (*a*) of D(R–H) shown in Table 3 from the activation energy (E) for the attack of bromine atoms on the alkanes, and the Polanyi relation $E = \alpha\Delta H + c$. The most probable value of α is 0·86. These values can now be

TABLE 3. D(R–H) *for alkanes at* 25° (*all kcal. mole*$^{-1}$).

Alkyl	E	Polanyi relation (*a*)	Polanyi relation (*b*)	This work	Electron-impact	$\Delta H_f°(R)$
Methyl	18·3	102·5	103·9	103·9	103·4	33·9
Ethyl	13·4	96·9	98·3	98·2	98·3	26·0
Neopentyl	14·3	97·9	99·3	—	—	7·5
Isopropyl	10·2	93·1	94·5	—	95·3	17·6
s-Butyl	10·2	93·2	94·6	—	—	12·3
t-Butyl	7·5	90·0	91·4	—	91·0	7·1

corrected (*b*) to correspond to the new value of $D(CH_3\text{–H})$. The agreement between $D(C_2H_5\text{–H})$ from the Polanyi relation and that found here is good. The agreement with the electron-impact values is also good. These bond strengths have been obtained from

[7] Christie, *Proc. Roy. Soc.*, 1958, *A*, **244**, 411.
[8] Fettis, Knox, and Trotman-Dickenson, *Canad. J. Chem.*, 1960, **38**, 1643.

those usually accepted for 0° K.[1] The last column of the Table lists the heats of formation of the radicals at 25°, from which many bond strengths can be derived.

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CHEMISTRY DEPARTMENT, EDINBURGH UNIVERSITY.
[Present address (A. F. T.-D.): EDWARD DAVIES CHEMICAL LABORATORY, ABERYSTWYTH.]
[*Received, March 3rd*, 1961.]

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582. *The Gaseous Oxidation of Isopropyl Alcohol. Part II.*[1] *Influence of the Surface on the Formation of Hydrogen Peroxide and Other Products.*

By A. R. BURGESS and C. F. CULLIS.

Studies of the gaseous oxidation of isopropyl alcohol have been carried out in Pyrex vessels treated with hydrofluoric acid and in a boric acid-coated vessel. Improved mixing of the reactants and an increased surface area of glass enhance the recovery of acetone but have little effect on the formation of peroxides. In a boric acid-coated vessel, the maximum yields of peroxides are lower than in Pyrex vessels but once such compounds are formed they are better preserved after long contact times. In order to account for these results it is necessary to distinguish between the effects of the different surfaces on HO_2 radicals and on hydrogen peroxide itself. The rate of reaction and the yields of peroxides increase as both types of surface are allowed to "age," and it has been shown that this effect is at any rate partly due to adsorption of water vapour.

IN Part I,[1] it was shown that the only products formed during the early stages of the gaseous oxidation of isopropyl alcohol are acetone and hydrogen peroxide. As reaction proceeds, however, the yield of hydrogen peroxide falls off sharply. Although some homogeneous decomposition of the peroxide takes place at the temperatures used,[2-6] the decrease in yield of peroxide is probably also partly due to breakdown of this compound at the surface of the vessel. The influence of the surface on the yields of hydrogen peroxide and other products formed during the reaction has therefore been studied.

EXPERIMENTAL

The flow apparatus and the experimental procedures have already been described in Part I. Three cylindrical Pyrex reaction vessels were used in this work; they were all 12 cm. long and 4·5 cm. in diameter. Vessel 1 was an open cylinder and had a surface : volume ratio of 1·07 cm.$^{-1}$. Vessel 2 was designed to improve mixing of the reactants and had six baffles placed at equal distances along its length; each of these contained one small hole, 1 mm. in diameter, which was placed near the circumference and at positions diametrically opposite in alternate baffles. The resulting surface : volume ratio of vessel 2 was 2·01 cm.$^{-1}$. Both vessels 1 and 2 were rinsed with hydrofluoric acid and washed three times with water before use. Vessel 3 was similar to vessel 1 but its surface was coated with a thick layer of boric acid.

RESULTS

(a) *The Effect of Re-mixing the Reacting Gases.*—In experiments with vessel 1, it was found that even after long reaction times the initial isopropyl alcohol was never completely used up.

[1] Part I, Burgess, Cullis, and Newitt, *J.*, 1961, 1884.
[2] McLane, *J. Chem. Phys.*, 1949, **17**, 379.
[3] Satterfield and Stein, *J. Phys. Chem.*, 1957, **61**, 538.
[4] Satterfield and Stein, *Ind. Eng. Chem.*, 1957, **49**, 1173.
[5] Giguère and Liu, *Canad. J. Chem.*, 1957, **35**, 283.
[6] Hoare, Protheroe, and Walsh, *Trans. Faraday Soc.*, 1959, **55**, 548.

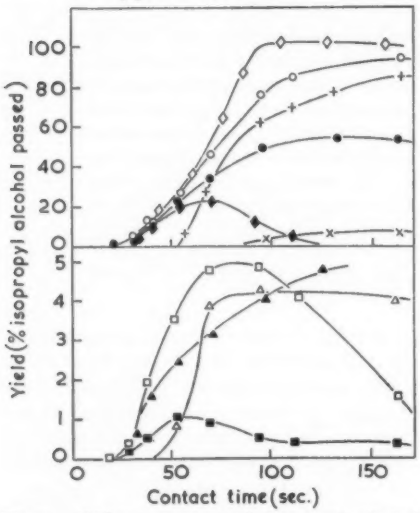
XUM

This is probably due to the fact that, in a flow system and with an open vessel, a small proportion of the reactants flows rapidly straight through the centre of the vessel before it has a chance to react. In vessel 2, in which the reactants and products were effectively re-mixed six times, a greater proportion of the alcohol was used up after long contact times, and the results obtained were much more reproducible. This vessel was therefore used for a detailed study of the reaction at 420° C.

Some typical results are given in Fig. 1 which shows the consumption of reactants and the formation of products for an equimolar isopropyl alcohol + oxygen mixture. The two reactants are used up at equal rates until about half the alcohol has reacted. Thereafter the oxygen is used up rather more rapidly, no doubt owing to secondary oxidation of intermediate products.

During the initial stages of reaction, acetone and peroxides (shown to be nearly exclusively hydrogen peroxide at 420°) are formed in almost 100% yield. Although these compounds

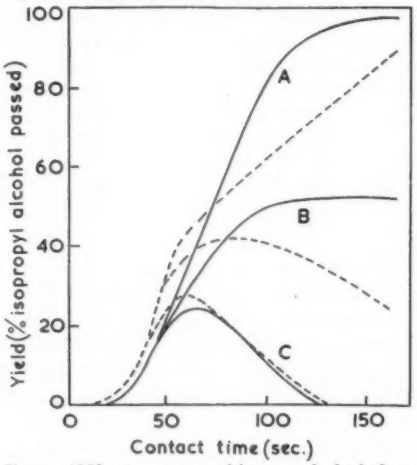
FIG. 1. *Consumption of reactants and formation of products in vessel 2.*



Temp. 420° c; pressure of isopropyl alcohol 75·3 mm.; of oxygen 78·8 mm.; of nitrogen 605·9 mm.

○ Isopropyl alcohol consumed; ◇ oxygen consumed; ● acetone; ◆ total peroxides; □ formaldehyde; ■ acetaldehyde; △ methyl alcohol; ▲ glyoxal; + carbon monoxide; × carbon dioxide.

FIG. 2. *Comparison of consumption of isopropyl alcohol* (A) *and of formation of acetone* (B) *and peroxides* (C) *in vessels 1 and 2.*



Temp. 420° c; pressure of isopropyl alcohol *ca.* 76 mm.; of oxygen *ca.* 76 mm.; of nitrogen *ca.* 608 mm.

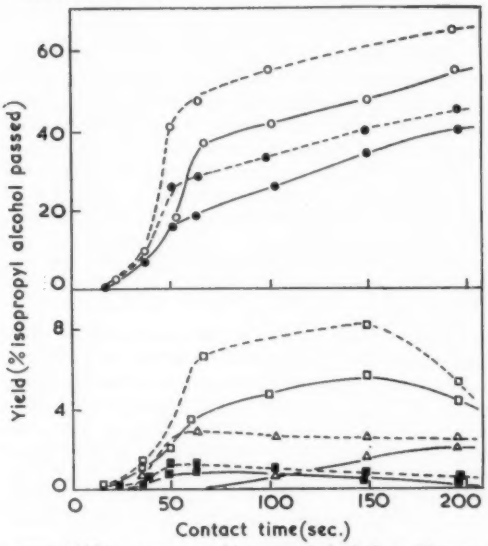
Broken line: vessel 1. Continuous line: vessel 2.

remain major products throughout, the efficiency of their formation starts to fall after about 20% of the reactants have been consumed, the yield of peroxide soon passing through a maximum and then decreasing again. Both formaldehyde and acetaldehyde appear quite early in the reaction, and the yields rise rapidly during the initial part of the autocatalytic stage, reaching a maximum at about the same time as the peroxide yield. Glyoxal too is formed quite early and its concentration rises steadily.

Methyl alcohol is not detectable until the middle of the autocatalytic stage, and it is then formed rapidly, the yield soon reaching a steady value of about 4%. Carbon monoxide starts to appear at about the same time, and by the end of reaction large amounts are present in the products; carbon dioxide is produced in much smaller quantities, probably arising from further oxidation of carbon monoxide.

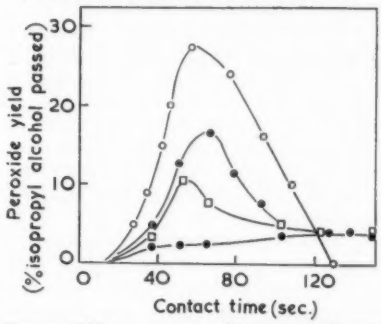
Fig. 2 compares the extents of alcohol consumption and of the yields of the two main products (acetone and hydrogen peroxide) in vessels 1 and 2. The induction period is the same but the maximum rate of oxidation is smaller in vessel 2. After *ca.* 70 sec., however, the alcohol

FIG. 3. *Comparison of consumption of reactant and of formation of products in "new" and "aged" boric acid-coated vessel.*



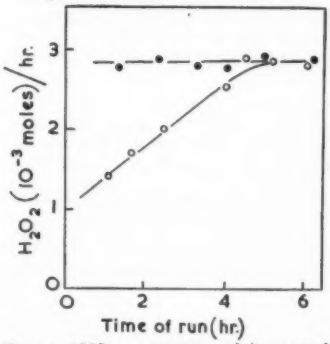
Temp. 420° c; pressure of isopropyl alcohol *ca.* 76 mm.; of oxygen *ca.* 76 mm.; of nitrogen *ca.* 608 mm.
Continuous line: "new" vessel 3. Broken line: "aged" vessel 3 (3—4 weeks).
○ Isopropyl alcohol consumed; ● acetone; □ formaldehyde; ■ acetaldehyde; △ methyl alcohol.

FIG. 4. *Comparison of formation of peroxide in uncoated and boric acid-coated vessels.*



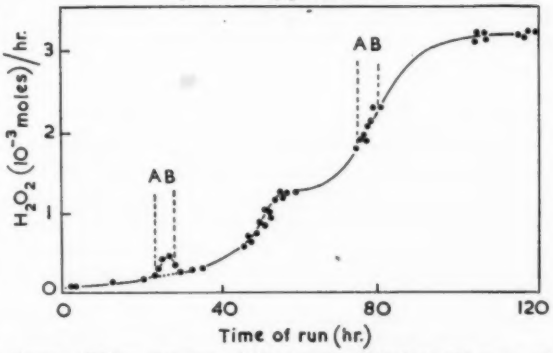
Temp. 420° c; pressure of isopropyl alcohol *ca.* 76 mm.; of oxygen *ca.* 76 mm.; of nitrogen *ca.* 608 mm.
○ "Aged" vessel 2; ● "new" vessel 3; □ "aged" vessel 3; ⊕ "aged" vessel 3 (samples taken after 5—6 hr.).

FIG. 5. *The influence of sampling time on the formation of peroxides in an "aged" boric acid-coated vessel.*



Temp. 420° c; pressure of isopropyl alcohol *ca.* 76 mm.; of oxygen *ca.* 76 mm.; of nitrogen *ca.* 608 mm.
○ Dry reaction mixture; ● reaction mixture containing 5·2 moles % of water vapour.

FIG. 6. *The influence of "ageing" of Pyrex glass surface on the formation of peroxides.*



Temp. 420° c; pressure of isopropyl alcohol *ca.* 76 mm.; of oxygen *ca.* 76 mm.; of nitrogen *ca.* 608 mm.; vessel 2.
A, water on; B, water off.

consumption is higher in this vessel and remains so until reaction is complete. The yield of acetone too is higher in vessel 2, and this compound appears to be better preserved under conditions of improved mixing. Despite the increased surface : volume ratio, the yield of peroxide is only slightly lower in vessel 2 and this suggests that in both the Pyrex vessels decomposition of hydrogen peroxide occurs mainly as a homogeneous process under the experimental conditions used.

(b) *The Effect of a Boric Acid Surface.*—In spite of the above conclusion, it was thought that it might be possible to minimise further the decomposition of hydrogen peroxide by use of a boric acid-coated vessel (vessel 3). Although it was expected that this would preserve peroxides more effectively, it was found that in a freshly-coated vessel, oxidation was much slower and yields of acetone, aldehydes, methyl alcohol, and peroxides were considerably lower (Figs. 3 and 4). Nevertheless, as the surface " aged " during 3—4 weeks, both the rate of oxidation of isopropyl alcohol and the amounts of the above products steadily increased. In the fully " aged " boric acid-coated vessel, the reaction rate was almost the same as in vessel 1, but the maximum yields of peroxide always remained somewhat lower (Fig. 4). The amount of peroxide remaining after long contact times was however greater in vessel 3 than in vessel 1, and this suggests that boric acid does in fact preserve hydrogen peroxide even though it is not conducive to its formation.

It was also noticed that when vessel 3 was fully " aged," yields of peroxides tended to be higher if the products were sampled after 5—6 hr. instead of after 1—2 hr. (Figs. 4 and 5). It was thought that this might be due to adsorption on the surface of the vessel of water vapour from the mixture of products and indeed when yields of hydrogen peroxide were measured as a function of the duration of the run, it was found that these increased up to *ca.* 6 hr. If, however, water vapour was artificially added to the mixture, after the surface had been allowed to attain its original condition, the maximum yield of peroxide was obtained immediately and no progressive increase occurred during a long run (Fig. 5). The vessel returned to its original condition after being evacuated for several hours at the reaction temperature so that the effect of water vapour is evidently not permanent.

(c) *The Effect of " Ageing " of Pyrex Glass.*—The effects noticed with vessel 3 prompted further study of the ageing of a Pyrex-glass surface. For this purpose an equimolar mixture of isopropyl alcohol and oxygen was passed continuously for several days through vessel 2 which had previously been washed with hydrofluoric acid; samples of products were collected every hour or so and analysed for peroxides. Some typical results are shown in Fig. 6. These suggest that " ageing " is a two-stage process and this belief is strengthened by observations of the effect of added water vapour during the two different stages. During the first stage, when water vapour was introduced into the reactant mixture, the yield of peroxide increased rapidly; when the water flow stopped, the yield immediately decreased again. On the other hand, addition of water vapour to the reactant mixture during the second stage of " ageing " did not exert any appreciable influence on the yields of hydrogen peroxide obtained.

Discussion

Much of the information at present available concerning the influence of the surface on gaseous oxidations is derived from detailed studies of the hydrogen + oxygen [7-9] and methane + oxygen [10-12] reactions. In the former, recent kinetic investigations [13-15] suggest that an aged boric acid surface is one of the most inert toward destruction of HO_2 radicals and of hydrogen peroxide. It has, too, been reported [2,16] that the use of boric acid-coated surfaces reduces to a minimum the heterogeneous decomposition of hydrogen peroxide.

[7] Willbourn and Hinshelwood, *Proc. Roy. Soc.*, 1945, *A*, **185**, 376.
[8] Egerton and Warren, *Proc. Roy. Soc.*, 1951, *A*, **204**, 465.
[9] Warren, *Proc. Roy. Soc.*, 1952, *A*, **211**, 86, 96.
[10] Hoare, *Trans. Faraday Soc.*, 1953, **49**, 628.
[11] Hoare and Walsh, Fifth Symp. Combustion, Reinhold Publ. Corp., New York, 1955, pp. 467, 474.
[12] Egerton, Minkoff, and Salooja, *Combustion and Flame*, 1957, **1**, 25.
[13] Baldwin and Mayor, *Rev. l'Inst. français Petrole*, 1958, **13**, 397.
[14] Baldwin and Mayor, Seventh Symp. Combustion, Butterworths, London, 1959, p. 8.
[15] Baldwin and Mayor, *Trans. Faraday Soc.*, 1960, **56**, 80, 93, 103.
[16] Cook, U.S.P. 2,368,640, 2,368,806.

On the other hand, other workers [3-6] have found that clean vitreous surfaces are in certain cases possibly even more suitable for the preservation of hydrogen peroxide and it has been suggested [17] that all acidic surfaces (including acid-treated vitreous materials which can be regarded as having a silicic acid coating [18]) should favour the formation of this compound since they facilitate conversion of HO_2 radicals into it.

In the present system, the largest amounts of peroxides are formed in acid-washed Pyrex vessels, and the extent of such a surface has relatively little effect on peroxide yields.[5] The results also indicate, however, that although boric acid helps to preserve hydrogen peroxide once it is formed, such a surface does not favour its production.[12] This suggests that, although the use of boric acid minimises decomposition of hydrogen peroxide, it is not as effective as an acid-treated vitreous surface in promoting the reaction: [17]

$$HO_2 + H^+ \longrightarrow \tfrac{1}{2}H_2O_2 + \tfrac{1}{2}O_2 + H^+$$

It is of interest that Broida,[19] from experiments on the second limit of the hydrogen + oxygen reaction, concluded that while a boric acid surface was the most inert toward the destruction of hydrogen atoms, Pyrex glass was the most effective material for the preservation of HO_2 radicals. Since probably only the latter species play a part in the gaseous oxidation of isopropyl alcohol, this may account for the greater yields of hydrogen peroxide formed in vessels 1 and 2 in the present system.

Surface " ageing " in oxidations generally leads to increased rates of reaction and to improved yields of peroxides. Such effects have frequently been ascribed to the adsorption of water vapour,[20] and Badin [21] has shown that in the $H + O_2$ reaction the yield of hydrogen peroxide varies with the " wetness " of the surface used. Voevodsky [22] suggested that adsorbed water vapour promotes the reaction:

$$HO_2 + H_2O \longrightarrow H_2O_2 + OH$$

although other workers [13-15] can find no support for such a process. There is certainly evidence that water vapour is strongly adsorbed by fused boric acid [5,12] and this probably accuents for the results now obtained with such a surface.

The experimental results show, however, that a similar hydration of a glass (silicic acid) surface is one of the causes of " ageing " effects shown in a Pyrex vessel. Nevertheless, even after full hydration has occurred, the " ageing " process can evidently continue so that it is clear that other factors are also involved. It is important to stress how difficult it is to draw general conclusions from results obtained for a particular system, for other workers [23,24] have shown that, in the propane + oxygen reaction, " ageing " of a Pyrex vessel leads to a steady decrease in rate of reaction and in peroxide yields.

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CHEMISTRY DEPARTMENT, IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, October* 31*st*, 1960.]

[17] Cheaney, Davies, Davis, Hoare, Protheroe, and Walsh, Seventh Symp. Combustion, Butterworths, London, 1959, p. 183.
[18] Cheaney and Walsh, *Fuel*, 1956, **35**, 258.
[19] Broida, *J. Chem. Phys.*, 1951, **19**, 790.
[20] Lewis and von Elbe, " Combustion Flames and Explosion of Gases," Academic Press, New York, 1951.
[21] Badin, *J. Amer. Chem. Soc.*, 1948, **70**, 3651.
[22] Voevodsky, *Zhur. fiz. Khim.*, 1946, **20**, 1285.
[23] Satterfield and Wilson, *Ind. Eng. Chem.*, 1954, **46**, 1001.
[24] Satterfield and Reid, Fifth Symp. Combustion, Reinhold Publ. Corp., New York, 1955, p. 511.

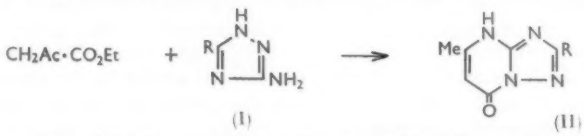
XUM

583. *The Structure of Certain Polyazaindenes. Part VIII.* Tetra-azaindenes derived from the Reaction of Ethyl β-Ethoxy-α-ethoxycarbonylcrotonate with 3-Amino-1,2,4-triazoles.*

By L. A. Williams.

The reaction of ethyl β-ethoxy-α-ethoxycarbonylcrotonate with 3-amino-1,2,4-triazoles can occur by two different routes, depending on the basicity of the medium. A number of tetra-azaindenes have been prepared by this reaction and their spectra compared.

3-Amino-1,2,4-triazole (I; R = H) and ethyl acetoacetate in acetic acid were shown by Bülow and Haas [1] to give a compound, m. p. 278°, which they formulated as the hydroxy-form of (II; R = H), although four isomeric structures for this compound are possible.

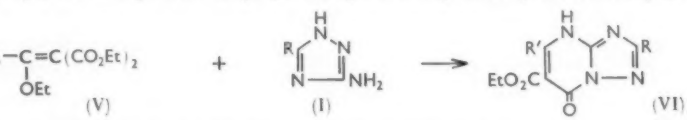


(I) (II)

Allen and his co-workers [2,3] later proved the structure (II) to be correct and prepared two further isomers (III; R = H) and (IV; R = H). They also showed [2] that 3-amino-1,2,4-triazole and ethyl β-ethoxy-α-ethoxycarbonylacrylate (V; R = H) in acetic acid or

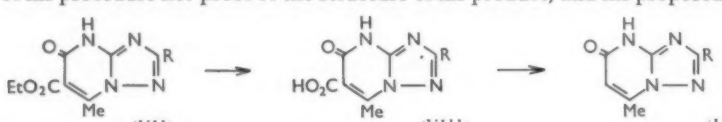
(III) (IV)

trichlorobenzene give a tetra-azaindene, to which they assigned, on the basis of its spectral characteristics, the structure (VI; R = R′ = H). Birr,[4] on the other hand, stated that the triazole (I; R = H) with ethyl β-ethoxy-α-ethoxycarbonylcrotonate (V; R = Me)



(V) (I) (VI)

gives a tetra-azaindene, to which he assigned structure (VII; R = H), which can be hydrolysed and decarboxylated to a compound isomeric with that obtained by Bülow and Haas. Reaction of the crotonate (V; R = Me) with the aminotriazole, like that described by Bülow and Haas, might give rise to four isomeric compounds. Birr gave neither details of his procedure nor proof of the structure of his product, and his proposed structure



(VII) (VIII) (IX)

is not that which might be expected by analogy with the work of Allen *et al.*[2] It, therefore, seemed desirable to examine the reaction further, and to compare the products with the three known isomers (II, III, and IV; R = H).

* Part VII, Reynolds and VanAllan, *J. Org. Chem.*, 1961, **26**, 115.

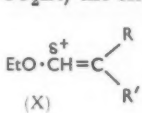
[1] Bülow and Haas, *Ber.*, 1909, **42**, 4638.
[2] Allen, Beilfuss, Burness, Reynolds, Tinker, and VanAllan, *J. Org. Chem.*, 1959, **24**, 779.
[3] Allen, Reynolds, Tinkers, Williams, and VanAllan, *J. Org. Chem.*, 1960, **25**, 361.
[4] Birr, *Z. wiss. Phot.*, 1952, **47**, No. 1—3, 2; see also Heimbach, B.P. 636,758.

Reaction of the triazole (I; R = H) with the crotonate (V; R = Me) in pyridine gave two isomeric esters. Only one of these formed a pyridinium salt, which was isolated by the addition of ether to the reaction mixture, and the free ester, m. p. 175°, was obtained by the acidification of an aqueous solution of this salt. The second ester, m. p. 208°, was obtained by chilling the ethereal filtrate. Both these esters were hydrolysed by 10% aqueous sodium hydroxide to acids, which were readily decarboxylated on melting or on boiling in quinoline or dimethylaniline. The ester, m. p. 175°, gives an acid, m. p. 212°, which on decarboxylation gives a compound, m. p. 278°, identified by mixed melting point and by ultraviolet and infrared absorption with the product of Bülow and Haas. This ester is, therefore, (VI; R = H, R′ = Me). The ester, m. p. 208°, on hydrolysis gives an acid, m. p. 228°, which, on decarboxylation, gives a compound, m. p. 266—267°, isomeric with that obtained by Bülow and Haas.

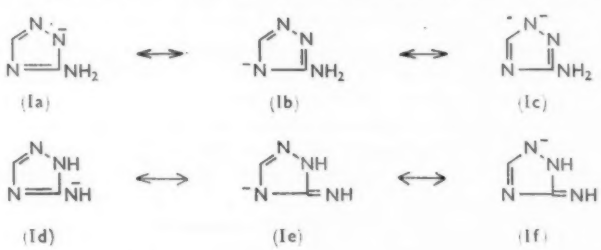
This compound differs from the isomers of (II) previously described in ultraviolet (Fig. 1) and infrared (Table 1) absorption and depresses their melting points.

Since the structures of the isomers (II, III, and IV; R = H) have been established [3] the new compound must have structure (IX; R = H), while the 5-ethoxycarbonyl and 5-carboxy-derivatives are represented by (VII) and (VIII) respectively.

Reaction of the crotonate (V; R = Me) with the aminotriazole (I; R = H) is an electrophilic attack by the ester on the triazole ring. The ester contains three electrophilic centres and it is not known which of these first attacks the nucleophilic centres of the triazole. Diels *et al.*[5] have shown, however, that in the related α-cyano-β-ethoxyacrylonitrile (X; R = R′ = CN) and ethyl α-cyano-β-ethoxyacrylate (X; R = CN, R′ = CO_2Et) the electrophilic centre at the β-carbon atom is the point of attack by nucleophilic reagents in addition-elimination reactions, with the subsequent displacement of the alkoxy-group. Kamlet [6] has also shown that methyl β-ethoxy-α-nitroacrylate (X; R = NO_2, R′ = CO_2Me) behaves similarly. In the crotonate (V), therefore, it would be reasonable to expect that the electrophilic β-carbon atom would be the most reactive towards nucleophilic attack.


(X)

It is also not known which of the nucleophilic centres of the triazole is the most reactive. It would be expected, however, that this aminotriazole, which shows some acidic properties, would be more reactive as its anion, *i.e.*, under basic conditions. Such anions would be expected to be of the form (Ia ⟷ b ⟷ c) rather than (Id ⟷ e ⟷ f)


(Ia) (Ib) (Ic)

(Id) (Ie) (If)

since the aromatic resonance in the former is degenerate. If so, one would expect that the more reactive (β) electrophilic centre of the crotonate (V) would, under basic conditions, react with a cyclic nitrogen atom, rather than with the free amino-group, to give the ester (VII). On the other hand, under acidic conditions, the active triazole species, which is presumably a cation, would be expected to be (Ig ⟷ h), and not (Ii) because of the near-degenerate resonance stabilisation of the former. Consequently, under acid conditions, the primary amino-group would be expected to be the most reactive nucleophilic centre.

[5] Diels, Gartner, Kaack, *Ber.*, 1922, **55**, 3439.
[6] Kamlet, *J. Org. Chem.*, 1959, **24**, 714.

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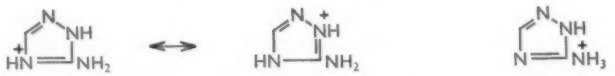
Irrespective of the nature of the more reactive electrophilic centre of the crotonate (V) it should, therefore, be possible to direct the attack on the triazole by the use of alkaline or acid conditions. The use of more strongly basic conditions than those given by pyridine as a solvent should favour even more strongly the formation of one of the isomeric esters.

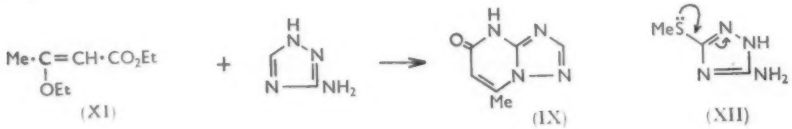


(Ig) (Ih) (Ii)

Indeed, the crotonate (V; R = Me) was found to react with the triazole (I; R = H) in alcohol in the presence of one equivalent of sodium ethoxide to give exclusively the ester (VII). In acidic conditions it would be expected that aminotriazole and the crotonate (V; R = Me) would give the ester (VI; R = H, R′ = Me), m. p. 175°. This was found to be the case, and apart from a small quantity of the acetyl derivative of the triazole (I) no other recognisable product was obtained.

From the above findings it can be concluded that in alkaline conditions the most highly nucleophilic centre in the triazole (I) is the $N_{(2)}$ atom.

The compound (III; R = H) is converted into its isomer (II; R = H) when heated in formic acid [7,8] or fused.[8] That no such isomerisation occurs during the decarboxylation of the acid (VIII; R = H) is established by the reaction of aminotriazole with ethyl β-ethoxycrotonate [9] (XI) in alcohol in the presence of an equivalent of sodium ethoxide, the compound (IX; R = H) being obtained. On the other hand, aminotriazole and the ethoxycrotonate (XI) react smoothly in acetic acid, to give only the compound (II; R = H).



(XI) (IX) (XII)

This sequence has been extended to reaction of the triazoles (I; R = SMe and NH_2) with the crotonate (V; R = Me), where it has been found that, in pyridine, the triazole I; R = SMe) reacts to give only the ester (VI; R = SMe; R′ = Me). This, if the above theory is correct, is to be expected since the $-M$ effect of the sulphur atom will decrease the acidity of the nucleus and thus make the formation of the anion (Ia) more difficult (cf. XII). In strongly basic conditions (sodium ethoxide) these two triazoles give the esters (VII; R = SMe and NH_2); these, after hydrolysis and decarboxylation, give the compounds (IX; R = SMe and NH_2) which are isomeric with those obtained by Fry.[10,11] The product of the condensation of the triazole (I; R = SMe) with ethyl acetoacetate in acetic acid was shown by Williams [12] to have structure (II; R = SMe). Two other isomers (III and IV; R = SMe) have been described by Allen *et al.*[3] The compound (IX; R = SMe), therefore, is the fourth of the isomers theoretically obtainable by the reaction described by Fry.

Spectrally these compounds show important similarities and differences. In the infrared region of the spectrum (Table 1) the findings of Allen *et al.*[2] that in the 6-oxo-compounds (IV; R = H and Me) the absorption band due to the amide-carbonyl group is at lower frequencies than for the isomers (II and III; R = H and Me), is confirmed for

[7] Allen, Beilfuss, Burness, Reynolds, Tinker, and VanAllan, *J. Org. Chem.*, 1959, **24**, 787.
[8] Shirakawa, *J. Pharm. Soc. Japan.*, 1958, **78**, 1395.
[9] Claisen, *Ber.*, 1895, **28**, 2731.
[10] Fry, B.P. 648,185.
[11] Fry, B.P. 648,184.
[12] Williams, *J.*, 1960, 1829.

compound (IX; R = H). In addition, the 4-oxotetra-azaindenes (II and III; R = H, SMe, and Me) differ from the 6-oxo-isomers (IV and IX) in showing an extra absorption band in the region of 1563—1575 cm.$^{-1}$ (Table 1) (see Allen *et al.*[2] for R = Me).

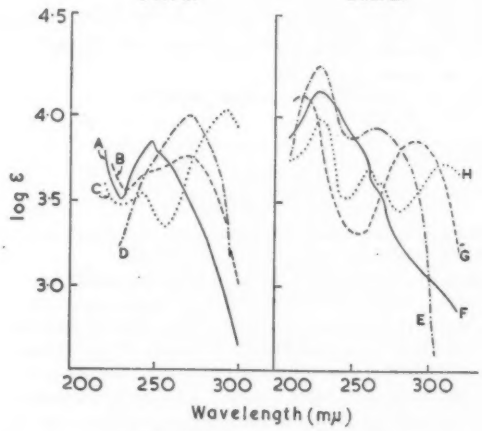
Further, the 1,3,3a,7-tetra-azaindenes are distinguished by a strong absorption band at 1325 cm.$^{-1}$ which is absent in the 1,2,3a,7-tetra-azaindenes. For the isomers (II and IX; R = SMe) this band, while still present, is less well developed.

TABLE 1. *Infrared absorption frequencies* (cm.$^{-1}$).

Compound	R	$\lambda_{max.}$	Compound	R	$\lambda_{max.}$	Compound	R	$\lambda_{max.}$	Compound	R	$\lambda_{max.}$
II	H	1695, 1600, 1563 s	II	SMe	1667, 1626, 1563 s	IX	H	1667, 1587 s	IX	SMe	1695, 1582 s
		1325 ms			1325 m			1325 s			1325 m
III	H	1724, 1626, 1575 s	III	SMe	1709, 1639, 1575 s	IV	H	1681, 1600 s	IV	SMe	1685, 1600 s

The ultraviolet absorption properties of the isomers (III and IV; R = H) in methanol and that of the isomer (II; R = H) in ammoniacal methanol have been described by Allen *et al.*[2,3] The absorptions of these compounds in methanol, together with that of the isomer (IX; R = H), are shown in Fig. 1, from which it is apparent that the 6-oxotetra-azaindenes absorb at lower extinction values than their 4-oxo-isomers. This is also the

FIG. 1. FIG. 2.



Ultraviolet absorption spectra of:

A, Compound IV, R = H. B, Compound IX, R = H. C, Compound III, R = H. D, Compound II, R = H. E, Compound II, R = SMe. F, Compound IV, R = SMe. G, Compound IX, R = SMe. H, Compound III, R = SMe.

case with the corresponding alkylthio-derivatives (Fig. 2). This is in agreement with Mason's findings [13] that with " nitrogen-containing heteroaromatic compounds containing two fused rings, *ortho*- and *para*-quinonoid conjugated systems may be qualitatively distinguished by the greater intensity of absorption in the long-wavelength band of the spectrum of the latter."

[13] Mason, *Chem. Soc. Special Publ.*, No. 3, p. 139.

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Allen *et al.* have shown that for 4-oxotetra-azaindenes the absorption of the long-wavelength band of the 1,2,3a,7-isomers is bathochromically displaced relative to the 1,3,3a,7-isomer. In the 6-oxo-series, however, the reverse situation prevails with the 1,3,3a,7-isomers absorbing at considerably the longer wavelengths.

Further, for compounds (II), as the electropositive nature of R increases, the position and extinction value of the long-wavelength band is only slightly affected, while with the isomers (IX) there is a pronounced bathochromic shift. Allen *et al.*[2] found a similar shift with the ester (VI; R = R′ = H).

The structures assigned to isomers (II, III, IV, and IX; R = H) are further supported by their nuclear magnetic resonance properties although the differences involved are rather small. The spectra (see Table 2) were determined at 56·4 Mc. in pyridine solutions (*ca.* 1%), with tetramethylsilane as an internal reference. The line positions given are

TABLE 2. *Nuclear magnetic resonance peaks.*

Compound	II	III	IX	IV
τ	7·69	7·69	7·57	7·63
J	0·7	—	1·1	1·1

τ values. Compounds (IX) and (IV) have the methyl group close to the five-membered ring and in each case the absorption is at slightly lower fields than for the isomers (II) and (III). This almost certainly reflects partial aromatic character of the five-membered ring.[13] The fact that the methyl peak for compound (IX) is slightly lower than for compound (IV) may be due to the proximity of the second nitrogen atom.

The coupling constants are probably characteristic of six-membered ring types (*i.e.*, 2-pyridone or 4-pyridone); the insolubility of the compound (III) prevented resolution of the doublet and hence J could not be measured.

A final point is that the 1,3,3a,7-tetra-azaindenes are stronger acids than the 1,2,3a,7-isomers. In the series (R = H) the 4-oxo-compounds are stronger acids than the 6-oxo-isomers (Table 3).

TABLE 3. *Acid strengths.*

Substance	R	10^7K_a at 20°	R	10^7K_a at 20°	Substance	R	10^7K_a at 20°	R	10^7K_a at 20°
II	H	5·8	SMe	5·3	IX	H	1·7	SMe	3·3
III	H	2·4	SMe	1·1	IV	H	1·3	SMe	1·4

EXPERIMENTAL

Ultraviolet absorptions are for methanol solutions; infrared measurements were made on potassium bromide discs; analyses are by Mr. C. B. Dennis.

Ethyl β-Ethoxy-α-ethoxycarbonylcrotonate (*Ethoxyethylidenemalonate*) (V; R = Me).—Ethyl orthoacetate (324 g., 2 mol.), ethyl malonate (320 g., 2 mol.), and sodium (2·3 g., dissolved in ethanol, 60 c.c.) were heated together in an oil-bath. The temperature was raised during 30—45 min. to 170° by which time alcohol began to distil; it was collected after fractionation through a short column. Heating was continued and the temperature raised as necessary to maintain distillation of the alcohol. After about 4 hr. (bath-temperature 205°) distillation of alcohol ceased (300 c.c. collected). The mixture was allowed to cool to 80°, a vacuum was applied, and heating was recommenced. A small fore-run (b. p. below 96/2 mm.) was obtained and discarded; the crude product was collected at 96—130°/2 mm. This fraction was re-distilled and the fraction boiling at 96—98°/2 mm. was collected and was purified further as described by McElvain and Burkett,[15] to give 220 g. of crystals, m. p. 25—27°, n^{20} 1·463 (Found: C, 57·5; H, 8·1. Calc. for $C_{11}H_{18}O_5$: C, 57·4; H, 7·8%).

Ethyl 4,7-Dihydro-6-methyl-4-oxo-1,3,3a,7-tetra-azaindene-5-carboxylate (VI; R′ = Me).—(1) 3-Amino-1,2,4-triazole (I; R = H) (4·2 g.) and ethyl β-ethoxy-α-ethoxycarbonylcrotonate (11·5 g.) were refluxed together in pyridine (30 c.c.) for 16 hr. After cooling, ether (90 c.c.) was added, and the mixture was shaken for about 2 min. The precipitate, a pyridinium salt, was collected and dissolved in cold water and filtered. The clear solution was acidified and the

[14] Elvidge and Jackman, *J.*, 1961, 859.
[15] McElvain and Burkett, *J. Amer. Chem. Soc.*, 1942, **64**, 1831.

solid collected and recrystallised from water and charcoal to give the *tetra-azaindene* (2 g.), m. p. 175° (Found: C, 48·3; H, 4·9; N, 25·6. $C_9H_{10}N_4O_3$ requires C, 48·6; H, 4·5; N, 25·3%).

(2) The triazole (I; R = H) (21 g.) and ester (V; R = Me) (57·5 g.) were heated in acetic acid (40 c.c.) for 3 hr. On cooling, a gelatinous precipitate was obtained, which, after trituration with ether, solidified. This was recrystallised from alcohol and then water, the filtrate being acidified with hydrochloric acid to give 23 g. of product, m. p. 175°.

Ethyl 6,7-*Dihydro*-4-*methyl*-6-*oxo*-1,3,3a,7-*tetra*-*azaindene*-5-*carboxylate* (VII).—(1) The ethereal filtrate obtained after removal of the pyridinium salt in method (1) above was chilled to 4° and after 3—4 hr. the *ester* was collected and recrystallised from water (charcoal); it had m. p. 208° (3 g.) (Found: C, 48·5; H, 4·9; N, 25·4%).

(2) The above reaction was repeated but including triethylamine (5 g., 1 mol.), and the mixture was refluxed overnight. After cooling, ether (60 c.c.) was added, and the solution chilled, to give ultimately the ester (VII) (4 g.), m. p. 208°.

(3) To sodium (4·6 g.) dissolved in alcohol (120 c.c.) 3-amino-1,2,4-triazole (16·8 g.) and ethyl β-ethoxy-α-ethoxycarbonylcrotonate (46 g.) were added. The mixture was refluxed for 6 hr., after which water (120 c.c.) was added. The solution was cooled rapidly and acidified with concentrated hydrochloric acid. The product (VII) was collected and recrystallised from water; it had m. p. 208° (26 g.).

4,7-*Dihydro*-6-*methyl*-4-*oxo*-1,3,3a,7-*tetra*-*azaindene*-5-*carboxylic Acid*.—The ester (VI; R′ = Me) (2 g.) was refluxed for 1 hr. in 10% aqueous sodium hydroxide (20 c.c.). After cooling, the solution was acidified with concentrated hydrochloric acid and chilled. The precipitated *acid* (1 g.), recrystallised from water, had m. p. 212° with evolution of carbon dioxide. The melt re-solidified and melted again without gas evolution at 278° (Found: C, 41·2; H, 3·5; N, 27·3. $C_7H_6N_4O_3,0{\cdot}5H_2O$ requires C, 41·4; H, 3·5; N, 27·5%. A redried sample gave N, 28·9. $C_7H_6N_4O_3$ requires N, 28·9%).

6,7-*Dihydro*-4-*methyl*-6-*oxo*-1,3,3a,7-*tetra*-*azaindene*-5-*carboxylic Acid* (VIII).—The ester (VII) (26 g.), hydrolysed as above, gave the *acid* (21 g.) (from water), m. p. 228—229° (evolution of carbon dioxide), re-solidified, remelted at 266—267° (Found: C, 43·6; H, 3·4; N, 29·7%).

6,7-*Dihydro*-4-*methyl*-6-*oxo*-1,3,3a,7-*tetra*-*azaindene* (IX).—(1) The acid (VIII) (5 g.) was melted under a vacuum at 280° with evolution of carbon dioxide, and the *product* sublimed into a short air-condenser. It (3 g.) recrystallised from water as plates, m. p. 266—267° (Found: C, 47·8; H, 4·1; N, 37·5. $C_6H_6N_4O$ requires C, 48·0; H, 4·0; N, 37·3%), $\lambda_{max.}$ 270 mμ (log ε 3·75).

(2) Ethyl β-ethoxycrotonate [9] (15·8 g.) was added to alcohol (100 c.c.) in which sodium (2·3 g.) had been dissolved then 3-amino-1,2,4-triazole (8·4 g.) was added. The mixture was refluxed for 24 hr., then water (100 c.c.) was added and the solution acidified and chilled to give the product (2·2 g.), as plates, m. p. and mixed m. p. 266—267°.

Ethyl β-ethoxycrotonate (15·8 g.) and 3-amino-1,2,4-triazole (8·4 g.) were refluxed together in glacial acetic acid (100 c.c.) for 4 hr. On chilling to 15° the product (10 g.) separated. Recrystallised from water, it melted at 278°, alone or mixed with the compound (II; R = H) prepared by the method of Bülow and Haas.[1]

Ethyl 6,7-*Dihydro*-4-*methyl*-2-*methylthio*-6-*oxo*-1,3,3a,7-*tetra*-*azaindene*-5-*carboxylate*.—To sodium (2·3 g.), dissolved in alcohol (60 c.c.), ethyl β-ethoxy-α-ethoxycarbonylcrotonate (23 g.) and 3-amino-5-methylthio-1,2,4-triazole (I; R = SMe) (13·0 g.) were added. The mixture was refluxed for 1·5 hr. by which time the whole had solidified. Water (60 c.c.) was added and the solution cooled and acidified with concentrated hydrochloric acid. The *ester* that crystallised was recrystallised from 50% acetic acid, forming needles, m. p. 214° (12 g.) (Found: C, 44·3; H, 4·6; N, 20·3; S, 11·9. $C_{10}H_{12}N_4O_3S$ requires C, 44·7; H, 4·8; N, 20·9; S, 11·9%).

This ester was hydrolysed as above to the *acid*, m. p. 235° (from water) (Found: C, 39·9; H, 3·6; N, 23·7; S, 13·3. $C_8H_8N_4O_3S$ requires C, 39·9; H, 3·7; N, 23·2; S, 13·3%).

6,7-*Dihydro*-4-*methyl*-2-*methylthio*-6-*oxo*-1,3,3a,7-*tetra*-*azaindene*.—The preceding acid was heated under a vacuum until the evolution of carbon dioxide ceased. The *product* recrystallised from water as needles, m. p. 280—281°, depressed to 234° on admixture with its isomers described by Fry [10] and Allen *et al.*[3] (Found: C, 42·2; H, 4·3; N, 28·9; S, 16·3. $C_7H_8N_4OS$ requires C, 42·6; H, 4·6; N, 28·4; S, 16·3%); it had $\lambda_{max.}$ 292 mμ (log ε 3·97).

Ethyl 4,7-*Dihydro*-6-*methyl*-2-*methylthio*-4-*oxo*-1,3,3a,7-*tetra*-*azaindene*-5-*carboxylate*.—3-Amino-5-methylthio-1,2,4-triazole (3·8 g.) and ethyl β-ethoxy-α-ethoxycarbonylcrotonate (6·8 g.) were refluxed together in pyridine (30 c.c.) for 4 hr. After cooling, ether (120 c.c.) was

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added and the mixture was chilled. The pyridinium salt which separated was collected and dissolved in water, and the solution was acidified. The *product* (1 g.) was collected and recrystallised from water as needles, m. p. 238° (0·75 g.) (Found: C, 44·5; H, 5·0; N, 21·5; S, 11·4%).

Ethyl 2-Amino-6,7-dihydro-4-methyl-6-oxo-1,3,3a,7-tetra-azaindene-5-carboxylate.—3,5-Diamino-1,2,4-triazole [16] (9·9 g.) and ethyl β-ethoxy-α-ethoxycarbonylcrotonate (23·0 g.) were refluxed in ethanol (60 c.c.) in which sodium (2·3 g.) had been dissolved. After 3—3·5 hr. water (60 c.c.) was added and the solution acidified. The solid *ester* (5 g.) was collected and recrystallised from water as needles, m. p. >300° (Found: C, 45·2; H, 4·7; N, 29·9. $C_9H_{11}N_5O_3$ requires C, 45·5; H, 4·6; N, 29·6%).

Hydrolysis as above gave an *acid* which, after suspension in boiling water to remove inorganic impurities, had m. p. >360° (Found: C, 40·0; H, 3·5; N, 33·5. $C_7H_7N_5O_3$ requires C, 40·2; H, 3·4; N, 33·5%).

2-Amino-6,7-dihydro-4-methyl-6-oxo-1,3,3a,7-tetra-azaindene.—The preceding amino-acid (1·5 g.) was heated under a vacuum until all had sublimed into a short air-condenser (the starting material did not melt previously). The *product* was collected and recrystallised from water as needles (0·9 g.), m. p. 357° (Found: C, 43·3; H, 4·4; N, 42·9. $C_6H_7N_5O$ requires C, 43·6; H, 4·2; N, 42·4%), $\lambda_{max.}$ 301 mμ (log ε 3·91).

The author thanks Messrs. B. S. Goode and I. Degan for the ultraviolet and infrared absorption measurements, Mr. J. H. Bridger for dissociation constants, Dr. E. B. Knott for helpful discussion, and Dr. L. M. Jackman for measurements and interpretation of the nuclear magnetic resonance spectra.

RESEARCH LABORATORIES, KODAK LIMITED,
HARROW, MIDDLESEX.

[*Received, November 18th,* 1960.]

[16] Hofmann and Ehrhart, *Ber.*, 1912, **45**, 2731.

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584. *Substituent Effects in Fluorene Compounds. Part III.*[1] *Hydrolysis of 9-Chloro-9-phenylfluorenes.*

By C. EABORN, R. C. GOLESWORTHY, and M. N. LILLY.

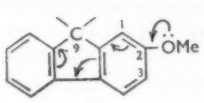
We have measured the rates of hydrolysis in 90% or 95% acetone (mainly in presence of an excess of lithium chloride) of 9-chloro-9-phenylfluorene and its derivatives having a methyl, methoxy-, or chloro-substituent in the *meta*- or *para*-position of the phenyl group or in the 2- or 3-position of the fluorenyl group. The effects of 2-substituents on the rate are close to those of *meta*-substituents, but the 2-methyl and 2-methoxy-compounds are slightly less reactive than their *meta*-analogues. The tautomeric release of electrons by the 2-methoxy-group is not significantly transmitted towards the 9-position through the unsubstituted ring.

The reactivities of 3-chloro- and 3-methyl-derivatives are not significantly different from those of their respective *para*-substituted analogues. The 3-methoxy-derivative is more reactive than the *p*-methoxy-derivative, but the difference is small relative to the overall effect of the substituent concerned.

THE aim of this series of investigations is to compare the electrical effects of substituents in the fluorene nucleus with those of substituents in the benzene ring. As far as effects at the 9-carbon atom are concerned, the simplest way of treating 2- and 3-substituents in fluorene is to assume that they are equivalent to *meta*- and *para*-substituents in toluene or its derivatives, but this may be incorrect for two reasons. First, the aromatic rings in fluorene are distorted from regular hexagons,[2] and the nature of the C–C bonds must

[1] Part II, Dickinson and Eaborn, *J.*, 1959, 3641.
[2] Brown and Bortner, *Acta Cryst.*, 1954, **7**, 139; Burns and Iball, *Nature*, 1954, **173**, 635.

be somewhat different from that of the bonds in benzene. Secondly, and at first sight possibly more importantly, tautomeric effects might be transmitted from the 2-position towards the 9-carbon atom through the unsubstituted ring, as in (I); such an effect was invoked by Arcus and Coombs [3] to explain the influence of substituents on the rearrangement of 9-fluorenyl azides to phenanthridines (see below). In the reaction of 9-bromofluorenes with potassium iodide in acetone,[4] and in oxime formation from 9-fluorenones,[1] 2-substituents were shown to have effects consistent with their being regarded as simple *meta*-substituents, but for the former reaction the possibility of some transmission of the $+T$ effect of the 2-methoxy-group by process (I) could not be excluded.



(I)

We have now measured the rates of hydrolysis in 90% aqueous acetone of a series of 9-chloro-9-phenylfluorenes having methyl, methoxy-, or chloro-groups in the 2- or 3-position of the fluorene nucleus or in the *meta*- or *para*-position of the phenyl group. This system has two considerable advantages: (i) the reaction is of the S_N1 type, and the presence in the transition state of an incipient carbonium ion adjacent to the rings can call forth the electromeric effects of substituents, and (ii) the influence of a group attached to the fluorene nucleus can be compared in absolute terms with the influence of the same group in the analogous position of the phenyl nucleus. In comparing effects of substituents in the fluorene system and in, say, the diphenylmethyl system, one can at best only hope to show that the effects on one system are *proportional*, on a free-energy of activation basis, to those in the other; no absolute comparison is possible because different reaction centres are involved in the two cases.

Hydrolytic S_N1 reactions of organic chlorides are frequently,[5] but not always,[6] retarded by common-ion salts, by added lithium chloride, for example, or by the hydrochloric acid formed in the hydrolysis. Such common-ion retardation is marked with 9-chloro-9-phenylfluorene (initially 0·01M) in 90% acetone; the calculated first-order constant falls by about 12% during the first 50% of reaction, while addition of 0·1M-lithium chloride lowers the rate by a factor of *ca.* 2·8. The initial rate is increased by a factor of 2·2 by the presence of 0·100M-lithium perchlorate which also causes the fall-off in rate constant during the first 50% of reaction to increase to *ca.* 22%. (The latter effect is explicable in terms of swamping-out of the ionic-strength effect of formed hydrochloric acid, which brings the common-ion effect into greater prominence.) The fall-off in first-order rate constant in absence of added salts is more marked the more reactive the chloride involved; the fall-off during the first 50% of reaction for some of the compounds is as follows: 3-Cl, 4%; *m*-MeO, 9%; 2-MeO, 8%; 2-Me, 14%; *p*-Me, 19%. No fall-off was observed for the *m*-chloro- and the 2-chloro-compound. (This effect can be understood in terms of increasing stability of the carbonium ion, which permits it to discriminate more effectively between the weakly nucleophilic water, present in high concentration, and the more strongly nucleophilic chloride ion present in low concentration. For a quantitative interpretation, of course, salt effects on the various reaction steps must be assessed.)

For reactions in absence of added salt, approximate rate constants at zero ionic strength can be obtained by extrapolation of a plot of the rate constant against the extent of reaction, and the results are shown as $k_1°$ in Table 1 (and also as rates, $k°_{rel}$, relative to that of the unsubstituted compound). But the uncertainty in such extrapolation was too great for our purposes,* and so we measured the rates in presence of lithium chloride

* In fact the pattern of substituent effects is much the same whether values or $k°_{rel}$ of k_{rel} (Table 1) are considered. A plot of log $k°_{rel}$ against log k_{rel} is a good straight line.

[3] Arcus and Coombs, *J.*, 1954, 4319.
[4] Dickinson and Eaborn, *J.*, 1959, 3574.
[5] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953, pp. 360—370.
[6] Bunton and Nayak, *J.*, 1959, 3854.

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(0·101M), which swamps the effect of chloride ion formed (0·01M for complete reaction) so that the first-order rate coefficients are constant throughout a run. (The added lithium chloride depresses the rate by a factor which increases with the reactivity of the organic chloride concerned, and thus there is a smaller spread of rates over the range of substituents.) The observed average first-order constants k_1 are shown in Table 1, along with the rates, k_{rel}, relative to that of 9-chloro-9-phenylfluorene. The reaction of the 3-methoxy-derivative was too fast in 90% acetone containing 0·101M-lithium chloride to be studied by our method, and so rates for 3-methyl, 3-methoxy-, and *p*-methoxy-derivatives were measured in 95% acetone containing 0·050M-lithium chloride, and the rate for the 3-methoxy-derivative in the former medium was calculated by assuming a linear free-energy relation between the rates in the two media. Any error introduced in this calculation is unimportant for our purposes.

TABLE 1. *Hydrolysis of 9-chloro-9-phenylfluorenes in 90% acetone at 25·0°.*

			In presence of 0·101M-LiCl					In presence of 0·101M-LiCl	
Substituent	$10^5k_1°$ (sec.$^{-1}$)	$k°_{rel}$	10^5k_1 (sec.$^{-1}$)	k_{rel}	Substituent	$10^5k_1°$ (sec.$^{-1}$)	$k°_{rel}$	10^5k_1 (sec.$^{-1}$)	k_{rel}
m-Cl	0·50	0·045	0·297	0·074	*m*-Me	19	1·7	5·91	1·47
2-Cl	0·49	0·045	0·289	0·072	2-Me	17	1·5	4·56	1·14
p-Cl	3·9	0·35	1·61	0·401	*p*-Me	78	7·1	19·4	4·83
3-Cl	4·5	0·41	1·64	0·409	3-Me	—	—	20·1	5·01
m-MeO	9·1	0·82	3·33	0·83	*p*-OMe	1250	110	260	64·5
2-MeO	6·2	0·56	2·67	0·67	3-OMe	—	—	(410) [a]	(102) [a]
None	11·1	1·00	4·01	1·00					

[a] Calculated (see text) from the following values of 10^5k_1 in 95% acetone containing 0·050M-LiCl: *p*-Me, 0·595; *p*-MeO, 25·8; 3-MeO, 48·4 sec.$^{-1}$.

The most important feature of the results is the relatively small difference between the effects of 2- as compared with *meta*-substituents and 3- as compared with *para*-substituents. However, some of the differences warrant discussion.

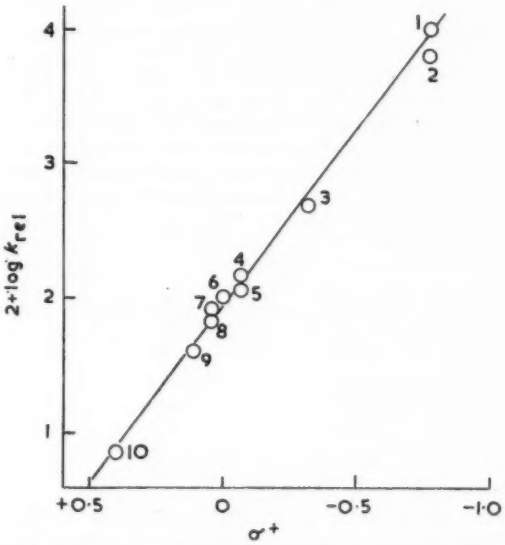
The 2-methyl and 2-methoxy-derivatives react slightly more slowly than the corresponding *meta*-substituted analogues (the difference between the 2- and *m*-chloro-compounds is within experimental error); clearly there is no significant transmission of the $+T$ effect of the 2-methoxy-group by process (I). If differences in the ease of transmission of inductive effects from *meta*- and 2-positions were important, the relative reactivity of 2- and *meta*-substituted compounds would be in one direction for methyl substituents (with $+I$ effects), and in the other for methoxy- and chloro-substituents (with $-I$ effects), and it seems that the lower reactivities of the 2-substituted compounds arises from a slightly poorer transmission of $+T$ effects towards the 9-position by secondary relay from positions conjugated with 2-substituents than from those conjugated with *meta*-substituents.

There is no significant difference between the reactivities of 3- and *para*-derivatives for chloro- and methyl substituents. The 3-methoxy-derivative is clearly more reactive than its *para*-analogue, but the difference is small relative to the overall effect of the substituent concerned. Since only the methoxy-group has a different effect from 3- and *para*-positions, it is likely that there is more effective transmission of the $+T$ effect towards the 9-position from the 3- than from the *para*-position. There is no obvious reason why this should be so, since there is no question of transmission of the $+T$ effect of a 3-methoxy-group towards the 9-position *via* the unsubstituted ring. Before speculating further on the nature of the effect of 3-substituents in fluorene we await results for other types of reactions and for additional substituents, particularly those having strong $-T$ effects.

The effects of substituents could be expected to correlate well with the σ^+ constants, since these are derived from an analogous reaction, the hydrolysis of αα-dimethylbenzyl chlorides in 90% acetone.[7] For the *meta*- and *para*-substituted compounds a plot of

[7] H. C. Brown and Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979.

$\log k_{rel}$ against σ^+ approximates to a straight line (see Figure); activation by the *p*-methoxy-group is somewhat less than expected from its σ^+ constant, and this may be a result of the small electron demand (as measured, for example, by the effect of a *p*-methyl group) in the hydrolysis of 9-chloro-9-phenylfluorenes when compared with the hydrolysis of αα-dimethylbenzyl chlorides. The $\log k_{rel}$–σ^+ plot for the 2- and 3-derivatives (σ^+ constants for *meta*- and *para*-substituents, respectively, being used) is a slightly better straight line. This illustrates that the observed differences between the effects of 2- and *meta*- or 3- and *para*-substituents are small compared with the variation in the effect of *meta*- and *para*-substitution even from one reaction to an analogous reaction. It also



Plot of $(2 + \log k_{rel})$ *for hydrolyses of chlorides against* σ^+. *Substituent in* 9-*chloro*-9-*phenylfluorene*: 1, 3-OMe; 2, *p*-OMe; 3, 3-Me and *p*-Me; 4, *m*-Me; 5, 2-Me; 6, H (unsubst.); 7, *m*-OMe; 8, 2-OMe; 9, 3-Cl and *p*-Cl; 10, 2-Cl and *m*-Cl.

emphasises the value of comparing effects in phenyl and fluorenyl systems directly within one structure, as we have done; had we measured only the effects of 2- and 3-substituents, and analysed these by use of σ^+ constants (or by direct comparison on a free-energy basis with other carbonium-ion-forming reactions of diphenylmethyl and other substituted-tolyl systems) we should have concluded that, relative to one another, the groups behaved exactly as though they were simple *meta*- and *para*-substituents in a benzene system, and should have missed the small but significant differences discussed above.

Since we conclude that electron-release by the 2-methoxy-group is not significantly transmitted towards the 9-position through the unsubstituted ring, it is important to consider Arcus and Coombs's evidence for such a process. They analysed the phenanthridine isomers formed from fluoren-9-ols on treatment with hydrazoic acid and sulphuric acid.[3] The rearrangement involved can be represented as (II) ⟶ (III). Electron supply towards the C–C bond to be broken assists the migration. Thus in a 2-substituted compound (IV), if the electron supply to the 8a–9 carbon bond is greater than that to the 9–9a bond, then the former bond migrates preferentially and 7-X-phenanthridine predominates over 2-X-phenanthridine in the product. From a 3-substituted fluorenol the 6- and 3-X-phenanthridines are correspondingly formed.

The experimental observations which need to be considered here are shown in Table 2. Arcus and Coombs concluded from the results that transmission of the $+I$ effect of the 2-methyl group to the 9–9a bond was approximately as effective as transmission of its $+T$ (hyperconjugation) effect to the 8a–9 bond by a process analogous to (I). The

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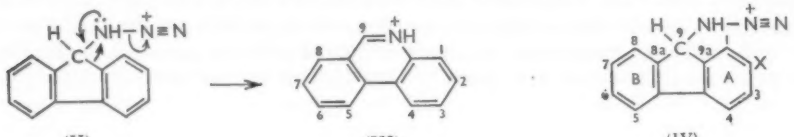
predominant migration of the B-ring in 2-methoxyfluorenol was taken to accord with inductive electron-withdrawal from 9–9a coupled with tautomeric electron-supply to 8a–9 by process (I). But it can equally satisfactorily be assumed that the substituents have no effect on the 8a–9 bond; the 2-methyl group would then have to activate the 9–9a bond by a factor of 1·13, and the 2-methoxy-, 2-nitro-, and 3-nitro-groups would



(II) (III) (IV)

have to deactivate the bond by factors of 2, 32, and 16, respectively. Within the limits of accuracy of the isomer proportions reported, these factors are quite consistent with the 2-substituents' acting as simple *meta*-substituents towards the 9–9a bond. It is true that the 3-nitro-group would then be expected to deactivate rather more than the 2-nitro-group (compare the σ^+ constants,[7] which should indicate the effects of *meta*- and *para*-groups in this type of rearrangement), but the experimental results do not, in fact, contradict this expectation because of the uncertainties in the isomeric compositions of the products.

TABLE 2.

Fluorenyl derivative	Total yield (%) of phenanthridine	Phenanthridine formed	Percentage of total yield (%)
2-NO_2	92	2-NO_2	3
		7-NO_2	97
3-NO_2	88	3-NO_2	6
		6-NO_2	94
2-MeO	32	2-MeO	32
		7-MeO	68
2-Me	81	2-Me	53
		7-Me	47

(For example, the phenanthridines from 2-nitrofluorenol were partly separated into 2- and 7-isomers by fractional crystallization, but 19% of the nitrophenanthridines was not recovered, and if allowance is made for this the proportion of 2-nitro-product is 2·5—21·5% and of 7-NO_2 product is 78·5—97·5%. If the proportion of 2-nitro-compound were 7%, this would mean that the 9–9a bond was deactivated only by a factor of 13.) In any case, the isomeric compositions quoted in Table 2 are even less in agreement with Arcus and Coombs's interpretations, for the 2-nitro-group, in addition to deactivating the 9–9a bond less effectively than the 3-nitro-group, should also deactivate the 8a–9 bond in a process analogous to (I), so that the proportion of migration of the B-ring should be markedly smaller for the 2-nitro- than for the 3-nitro-fluorenol. But the uncertainty in the isomer proportions reported by Arcus and Coombes renders further speculation unfruitful, and we can merely conclude that their inference of electron transmission of type (I) was unjustified.

EXPERIMENTAL

Materials.—Acetone was purified and dried by Conant and Kirner's method.[8] One volume of water was made up to 10 or 20 volumes with acetone to give 90% or 95% acetone, respectively.

9-Phenylfluoren-9-ols containing substituents in the phenyl group were prepared from fluoren-9-one and the appropriate arylmagnesium bromide in ether.[9,10] The insoluble complex formed was separated and washed with ether before being hydrolysed with dilute hydrochloric acid.[9] The fluorenols were extracted with benzene, the extract was concentrated and diluted

[8] Conant and Kirner, *J. Amer. Chem. Soc.*, 1924, **46**, 245.
[9] Ullman and von Wurstemberger, *Ber.*, 1904, **37**, 73.
[10] Williamson, Anderson, and Watt, *J. Amer. Chem. Soc.*, 1943, **65**, 49.

with a little light petroleum, and the resulting precipitate was recrystallized from light petroleum (b. p. 60—80°). The properties of the 9-(X·C_6H_4)·$C_{13}H_8$·OH-9 compounds were as follows: (X=) H, m. p. 85° (but 109° when examined several months later; cf. refs. 9 and 11); *m*-Cl, m. p. 81—82° (Found: C, 78·9; H, 4·4. $C_{19}H_{13}OCl$ requires C, 78·2; H, 4·5%); *p*-Cl, m. p. 91—92° (Found: C, 78·3; H, 4·6%); *m*-Me, m. p. 81·5—82·5° (Found: C, 88·5; H, 6·1. $C_{20}H_{16}O$ requires C, 88·2; H, 5·9%); *p*-Me, m. p. 85·5—86·5° (Found: C, 87·8; H, 5·9%); *m*-MeO, m. p. 89—90° (Found: C, 83·5; H, 5·5. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·6%); *p*-MeO, m. p. 130—132° (Found: C, 83·9; H, 6·2%). A m. p. of 87—88° has been recorded [12] for the last compound. Our sample gave poor analysis figures, but yielded the 9-chloro-compound on the usual treatment described below.

The above fluorenols were treated with hydrogen chloride in benzene in presence of calcium chloride,[13] and the resulting solution was filtered and concentrated at reduced pressure in a stream of hydrogen chloride. Addition of light petroleum gave 9-aryl-9-chlorofluorenes which, after recrystallization from light petroleum (b. p. 60—80°) with exclusion of moisture, had the following properties: (X=) H, m. p. 79° (lit.,[10,13,14] 79·5°); *m*-Cl, m. p. 72·5—73° (Found: hydrolysable Cl, 11·3. $C_{19}H_{12}Cl_2$ requires 1Cl, 11·4%); *p*-Cl, m. p. 79·5—80·5° (Found: hydrolysable Cl, 11·4%); *m*-Me, m. p. 83·5—84·5° (Found: hydrolysable Cl, 12·1. $C_{20}H_{15}Cl$ requires Cl, 12·2%); *p*-Me, m. p. 97° (lit.,[15] 96—97°) (Found: hydrolysable Cl, 12·1%); *m*-MeO, 108·5—109° (Found: hydrolysable Cl, 11·5. $C_{20}H_{15}ClO$ requires Cl, 11·55%); *p*-MeO, m. p. 151·5—152·5° (lit.,[12,16] 149—151°) (hydrolysable Cl, 11·4%).

9-Phenylfluoren-9-ols with substituents in the fluorene nucleus were prepared from the corresponding fluoren-9-ones [17] and phenylmagnesium bromide in ether, but were usually not isolated. The precipitated complex formed in the coupling was filtered off, washed with ether, and then hydrolysed in the usual way in presence of ether. The ether was replaced by benzene, and water was removed by azeotropic distillation. The benzene solution was then treated with hydrogen chloride in presence of calcium chloride to give substituted 9-*chloro*-9-*phenylfluorenes*, which, after recrystallization from light petroleum (b. p. 60—80°) had the following properties: 2-Cl, m. p. 106·5—107° (Found: C, 73·5; H, 4·0; hydrolysable Cl, 11·3. $C_{19}H_{12}Cl_2$ requires C, 73·5; H, 3·9; 1Cl, 11·4%); 3-Cl, m. p. 112—113° (Found: C, 73·4; H, 3·9; hydrolysable Cl, 11·4%); 2-Me, m. p. 100·5—101·5° (Found: C, 82·6; H, 5·3; hydrolysable Cl, 11·8. $C_{20}H_{15}Cl$ requires C, 82·6; H, 5·2; 1Cl, 12·2%); 2-MeO, m. p. 88·5—89° (Found: C, 78·3; H, 5·0; Cl, 11·8; 1Cl, 11·3. $C_{20}H_{15}ClO$ requires: C, 78·3; H, 4·9; 1Cl, 11·55%).

3-Methoxy-9-phenylfluoren-9-ol was isolated in 75% yield and recrystallized from light petroleum to a m. p. of 83—84° (lit.,[12] m. p. 84°). It was converted into the 9-chloro-compound in the usual way, but recrystallization gave a solid of m. p. 225°, containing no hydrolysable chlorine. However, recrystallization of the freshly prepared chloride from light petroleum containing acetyl chloride gave 9-chloro-3-methoxy-9-phenylfluorene, m. p. 118° (lit.,[12] m. p. 119°) (Found: C, 78·5; H, 5·0; hydrolysable Cl, 11·5. Calc. for $C_{20}H_{15}ClO$: C, 78·3; H, 4·9; 1Cl, 11·55%).

9-Chloro-3-methyl-9-phenylfluorene was not obtained pure in spite of several attempts, and the sample used for rate measurements was obtained by removal of the benzene in a stream of hydrogen chloride from a solution obtained by treating the alcohol with hydrogen chloride in the usual way; the sample contained only 82% of the calculated amount of hydrolysable chlorine, but its hydrolysis showed satisfactory first-order kinetics. Attempts to purify this and other samples by recrystallization gave material containing no hydrolysable chlorine; for example, recrystallization from light petroleum containing acetyl chloride gave a hydrocarbon of m. p. 110·5—111·5° (Found: C, 93·55; H, 6·55%).

Hydrolysis Products.—For a few typical 9-chloro-9-(X-phenyl)-fluorenes, hydrolysis was shown to give the corresponding alcohols substantially pure. A solution of the chloride in 90% acetone was set aside for an appropriate time and then added to excess of water. The mixture was kept in a refrigerator until the precipitated oil had crystallized, and the crystals were removed and dried and their m. p.s were found, with the following results: phenyl, m. p.

[11] Bachmann, *J. Amer. Chem. Soc.*, 1930, **52**, 3287; Arcus and Coombs, *J.*, 1954, 3977.
[12] Gomberg and Buchler, *J. Amer. Chem. Soc.*, 1923, **45**, 207.
[13] Gomberg and Cone, *Ber.*, 1906, **39**, 2957.
[14] Kliegl, *Ber.*, 1905, **38**, 284.
[15] Schniepp and Marvel, *J. Amer. Chem. Soc.*, 1935, **57**, 1635.
[16] Schlenk and Mair, *Annalen*, 1912, **394**, 198.
[17] Dickinson and Eaborn, *J.*, 1959, 2337.

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108°; *m*-chlorophenyl, m. p. 80·0°; *p*-methylphenyl, 86·0°; *m*-methoxyphenyl, 88·5°. From 9-chloro-3-methoxy-9-phenylfluorene a solid of m. p. 83·5° was similarly obtained.

Rate Measurements.—Sufficient of the 9-chloro-9-phenylfluorene to give a *ca.* 0·01M-solution was weighed into a 50-ml. graduated flask, which was then placed in a thermostat at 25·0° ± 0·04°. Solvent, with or without dissolved lithium chloride, pre-heated to 25·0°, was added to the mark, the flask being shaken vigorously, still immersed in the thermostat, during and immediately after the addition. The solid normally dissolved within a few seconds. Aliquot parts (usually 5 ml.) were withdrawn at suitable times (usually measured from completion of the addition of the solvent to the chloride, but sometimes from the time of removal of the first sample) and added to 50 ml. of acetone which had been cooled in ethanol–solid carbon dioxide, the time of half-addition being noted. The cold solution was quickly titrated against standard aqueous sodium hydroxide with lacmoid as indicator. For the fastest runs, involving the *p*-methoxy-derivative in 90% acetone in absence of lithium chloride, the moments of removal of samples were noted verbally on a tape-recorder and the times subsequently derived on play-back. The quenched samples were stored at −78° until the end of the reaction, and then titrated.

First-order rate constants, k_1, were obtained from plots of t against log $(T_\infty - T_t)$, but in the typical runs below have been calculated directly from the equation $k_1 t = 2{\cdot}303 \log [(T_\infty - T_0)/(T_\infty - T_t)]$ where T_0 is the titre at " zero " time (see above), T_t the titre at time t, and T_∞ that at complete reaction. The value of T_∞ was obtained either from a reaction mixture left at 25·0° for at least 10 half-lives, or, in the case of slower reactions by adding water (insufficient to cause precipitation but sufficient to speed-up hydrolysis considerably) to a 5 ml. sample and keeping the mixture at 25° for a short time before adding it to acetone for titration.

The following runs are typical. (*a*) 9-Chloro-9-*m*-tolylfluorene (0·137 g.) in 50 ml. of 90% acetone.

t (min.)	0	12	26	43	58	104	137	185	∞
Ml. of 0·00520M-NaOH	0·260	1·345	2·330	3·340	4·05	5·710	6·550	7·390	9·225
$10^5 k_1$ (sec.$^{-1}$)	—	17·9	16·8	16·3	15·8	15·0	14·7	14·3	—

Times were measured from that for the first sample. Extrapolation to zero titre gave a value for $k_1{}^\circ$ of 19×10^{-5} sec.$^{-1}$.

(*b*) 9-Chloro-9-*m*-tolylfluorene (0·160 g.) in 50 ml. of 90% acetone containing 0·101M-LiCl; times measured from mixing of reactants.

t (min.)	30	66	150	250	400	∞
Ml. of 0·00520M-NaOH	0·545	1·090	2·130	3·055	3·965	5·205
$10^5 k_1$ (sec.$^{-1}$)	6·01	5·93	5·83	5·84	5·98	—

(*c*) 9-Chloro-9-*p*-methoxyphenylfluorene (0·125 g.) in 50 ml. of 95% acetone containing 0·0500M-LiCl; times measured from mixing of reactants.

t (min.)	15	30	67	98	161	∞
Ml. of 0·0106M-NaOH	0·80	1·41	2·41	2·85	3·46	3·77
$10^5 k_1$ (sec.$^{-1}$)	26·4	26·0	25·4	26·3	25·7	—

The rate constants quoted in Table 1 are in most cases the mean of values obtained graphically from three independent runs on each compound. Rate constants could normally be duplicated to within ±1·5% for runs in 90% or 95% acetone containing lithium chloride. Rate constants for these media are believed to be accurate to within ±3% except possibly for (i) the *p*-methoxy-derivative in 90% acetone containing 0·101M-LiCl, since reaction was so fast that the error in k_1 could be as large as ±10%, and (ii) the 3-methyl derivative, which was impure, but which gave good first-order kinetics.

Values of k° determined in 90% acetone in absence of lithium chloride cannot be regarded generally as accurate to better than ±10% because of the extrapolation involved, but the error is probably smaller with less reactive chlorides for which the rate constant did not fall much during a run.

We thank Mr. P. Gilliver who prepared some of the fluorene derivatives used.

THE UNIVERSITY, LEICESTER. [*Received, January 18th*, 1961.]

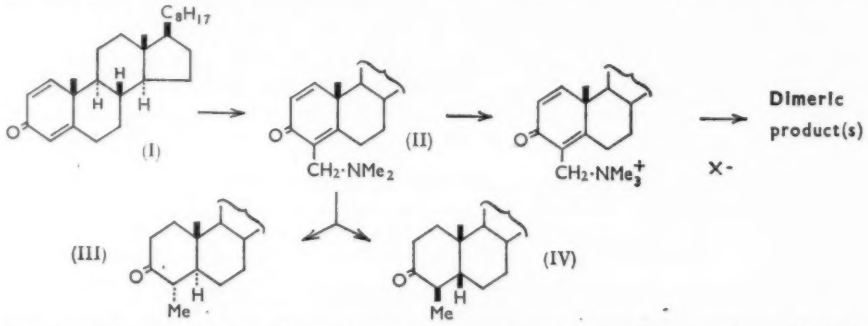
585. *The Mannich Reaction with Cholesta-1,4-dien-3-one.*

By G. I. Gregory and A. G. Long.

4-Dimethylaminomethylcholesta-1,4-dien-3-one has been prepared from cholesta-1,4-dien-3-one, formaldehyde, and dimethylamine hydrochloride. From the hydrogenation of this Mannich base 4α-methyl-5α-cholestan-3-one and 4β-methyl-5β-cholestan-3-one were isolated. Of the several by-products formed during the Mannich reaction one has been identified as the formal of 2-hydroxymethyl-4-methyl-19-norcholesta-1,3,5(10)-trien-1-ol. An attempt to apply the Hofmann degradation to the methiodide of 4-dimethylaminomethylcholesta-1,4-dien-3-one gave rise to a non-basic dimer or mixture of dimers of undetermined structure.

In our search for new methods of introducing methyl groups into the steroid nucleus we made several unsuccessful attempts to introduce substituents at position 6 in cholesta-1,4-dien-3-one (I) by base-catalysed reaction with methyl iodide and by Knoevenagel condensation with benzaldehyde. Finally we considered the Mannich reaction on 1,4-dien-3-ones as a means of introducing a dimethylaminomethyl group at the 6-position, which we hoped to be suitably activated (*e.g.*,[1] introduction of a bromine atom at position 6 in 1,4-dien-3-ones). We do not know [2] of any examples of substitution of an αβ-unsaturated ketone in the γ-position during the Mannich reaction.

Cholesta-1,4-dien-3-one (I), when treated with dimethylamine hydrochloride and formaldehyde under the usual conditions for the Mannich reaction,[2] gave a low yield of



basic products. In view of the success of acetic acid as solvent in the aminomethylation of, *e.g.*, ferrocene,[3] indole,[4] and acetone,[5] we refluxed cholesta-1,4-dien-3-one (I) with dimethylamine hydrochloride and formaldehyde in glacial acetic acid and isolated an oily basic fraction and a neutral fraction. The oily base gave an oxalate, platinichloride and methiodide, and analyses indicated that it was monoacidic and contained a $CH_2{\cdot}NMe_2$ group in the cholesta-1,4-dien-3-one framework. The ultraviolet absorption maximum was at 242 mμ (near those for unsubstituted 1,4-dien-3-ones and 4-methyl-[6] and 6α-methyl-1,4-dien-3-ones;[7] known 2-methyl-1,4-dien-3-ones[8] show $\lambda_{max.}$ 245—248 mμ). Peaks at

[1] Romo, Djerassi, and Rosenkranz, *J. Org. Chem.*, 1950, **15**, 896.
[2] Reichert, "Die Mannich-Reaktion," Springer Verlag, Berlin, 1959; Schröter, "Methoden der Organischen Chemie," Houben-Weyl (Band 11, Teil 1), Georg Thieme Verlag, Stuttgart, 1957, pp. 731 *et seq.*; Blicke, "Organic Reactions," Vol. I, 1942, pp. 303 *et seq.*
[3] Lindsay and Hauser, *J. Org. Chem.*, 1957, **22**, 355.
[4] Snyder and Eliel, *J. Amer. Chem. Soc.*, 1948, **70**, 1703.
[5] Blicke and McCarty, *J. Org. Chem.*, 1959, **24**, 1376.
[6] Sondheimer and Mazur, *J. Amer. Chem. Soc.*, 1957, **79**, 2906.
[7] Spero, Thompson, Magerlein, Hanze, Murray, Sebek, and Hogg, *J. Amer. Chem. Soc.*, 1956, **78**, 6213; Spero, Thompson, Lincoln, Schneider, and Hogg, *ibid.*, 1957, **79**, 1515; Fried, Arth, and Sarett, *ibid.*, 1959, **81**, 1235.
[8] Iriarte and Ringold, *Tetrahedron*, 1958, **3**, 28; Bernstein, Heller, Littell, Stolar, Lenhard, Allen, and Ringler, *J. Amer. Chem. Soc.*, 1959, **81**, 1696.

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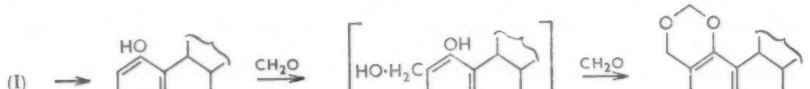
1660, 1628, 856, and 820 cm.$^{-1}$ in the infrared spectra suggested that the substituent was at position 4, for a similar absorption pattern is reported [6] for 1,2-dehydro-4-methyltestosterone. Introduction of the $CH_2{\cdot}NMe_2$ group into the ketone (I) had increased the molecular rotation by +128°. In general, 6α-methyl- [7] and 2-methyl-1,4-dien-3-ones [8] have a lower molecular rotation than their unsubstituted analogues; [7] on the other hand introduction of a 4-methyl group into 4-en-3-ones or 1,4-dien-3-ones [6] enhances the molecular rotation. The physical properties of our base thus favoured its formulation as 4-dimethylaminomethylcholesta-1,4-dien-3-one (II) although the analogies, derived as they are from the properties of methyl-steroids, were too tenuous to constitute structural proof.

Conclusive evidence for structure (II) came from a study of the reduction of the compound. Hydrogenation (3 mol.) of the purified base over palladium or Raney nickel in ethyl acetate or benzene provided a nitrogen-free, neutral product showing a single unconjugated ketone absorption in the infrared region. The product was separated into 4α-methyl-5α- [9,10] (III) and 4β-methyl-5β-cholestan-3-one [10] (IV). A careful search failed to detect the presence of 4β-methyl-5α-cholestan-3-one, which had been isolated [10] together with its isomers (III) and (IV) from the product of hydrogenation of 4-methylcholest-4-en-3-one.

Hydrogenation of the base (II) in acetic acid over platinum resulted in the uptake of 3 mol. of hydrogen, giving a basic oil. The infrared spectrum showed the absence of ketone absorption and the presence of a strongly hydrogen-bonded hydroxyl group. We have not characterised this product further but suggest that it is a mixture of isomeric 4-dimethylaminomethylcholestan-3-ols.

Boiling an aqueous solution of the methohydroxide (VI) of the Mannich base (II) gave a nitrogen-free, neutral glass. Attempts to purify this failed to yield fractions with properties significantly different from those of the crude material. The ultraviolet ($\lambda_{max.}$ 237, 271 infl. mμ) and infrared ($\nu_{max.}$ 1656, 1624, 830, and 800 cm.$^{-1}$) spectra were



(VII) (VIII)

not readily fitted to known conjugated-ketone absorptions. Ozonolysis of this product gave formaldehyde, suggesting the presence of a methylene group. The Rast method gave a molecular weight of 810, indicating that the product is dimeric. There are many precedents for such a dimerisation among simpler α-methylene-ketones.[2,11]

Reaction of the dienone (I) with paraformaldehyde and dimethylamine hydrochloride in acetic acid provided, besides the base (II), a neutral oil. Chromatography furnished a new crystalline compound, whose high specific rotation and characteristic ultraviolet spectrum suggested that it contained an aromatic ring.[1,12,13] The infrared spectrum proved the absence of hydroxy- and keto-groups, but provided strong evidence for the presence of a ketal ($\nu_{max.}$ 1240, 1102, 1050, and 1018 cm.$^{-1}$). The absorption due to the aromatic ring suggested [14] the presence of one unsubstituted C–H bond ($\nu_{max.}$ 856 cm.$^{-1}$).

[9] Meakins and Rodig, *J.*, 1956, 4679; Beton, Halsall, Jones, and Phillips, *J.*, 1957, 753; Djerassi, Mills, and Villotti, *J. Amer. Chem. Soc.*, 1958, **80**, 1005.
[10] Mazur and Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.
[11] *E.g.*, Pummerer and Cherbuliez, *Ber.*, 1919, **52**, 1392; Romann, Frey, Stadler, and Echenmoser, *Helv. Chim. Acta*, 1957, **40** 1900.
[12] Inhoffen and Huang-Minlon, *Naturwiss.*, 1938, **26**, 756; Inhoffen and Zühlsdorff, *Ber.*, 1941, **74**, 604; Wilds and Djerassi, *J. Amer. Chem. Soc.*, 1946, **68**, 1712; Woodward, Inhoffen, Larson, and Menzel, *Chem. Ber.*, 1953, **86**, 594.
[13] Dreiding, Pummer, and Tomasewski, *J. Amer. Chem. Soc.*, 1953, **75**, 3159.
[14] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen, London, 2nd edn., 1958, p. 79.

A colour test [15] for a 1,3-dioxen was positive whereas the phenol (VII) and several other steroids did not give the test (see Experimental section). These properties are consistent with a compound of structure (VIII) that may arise by aromatisation of cholesta-1,4-dien-3-one (I) to 4-methyl-19-norcholesta-1,3,5(10)-trien-1-ol (VII), subsequent hydroxymethylation at the *ortho*-position (2), and formation of the dioxen with a second molecule of formaldehyde. In order to discount structures arising from a similar sequence of reactions with alternative rearrangement products [1,6,13,16] we subjected the triene (VII) to the conditions used to prepare the Mannich base (II). Chromatography of the product yielded a single formal having properties identical with those of the by-product (VIII).

An attempted acid-catalysed dienone–phenol rearrangement of 4-dimethylaminomethylcholesta-1,4-dien-3-one (II) failed under conditions that had furnished a high yield of the phenol (VII) from cholesta-1,4-dien-3-one (I). This may be attributed to the proximity of the positively charged ammonium ion to the ketone group; protonation of the latter, which necessarily precedes aromatisation,[1,12,13,17] is thus hindered.

Experimental

Unless other conditions are specified, solutions in chloroform (18—22°, 0·5—1·5%), ethanol, and carbon disulphide, respectively, were used for measurements of optical rotation, and of ultraviolet and infrared spectra; m. p.s were measured on a Kofler block and are uncorrected; products were dried in solvents with anhydrous magnesium sulphate; alumina (Hopkin and Williams MFC grade, Brockmann Activity Grade I) was used for chromatography.

Reaction of Cholesta-1,4-dien-3-one (I) *with Formaldehyde and Dimethylamine Hydrochloride.*—The dienone [12] (I) (10·0 g.), 36% aqueous formaldehyde (10·9 ml., 5 equiv.), and dimethylamine hydrochloride (10·65 g., 5 equiv.) were heated in refluxing acetic acid (200 ml.) for 18 hr. The initially colourless solution had become light orange-brown. As much as possible of the solvent was evaporated at 100° *in vacuo*; then toluene (2 × 200 ml.) was evaporated likewise. Addition of water and continuous ether-extraction led to a brown neutral oil (A) (2·4 g.) (see below).

The aqueous phase from the extraction was adjusted to pH 9—10 with sodium carbonate, then re-extracted continuously with ether, giving a basic fraction B as a light brown oil (5·5 g.). When the aqueous phase from this separation was made strongly alkaline with 40% sodium hydroxide solution a bright yellow precipitate,[18] insoluble in ether, was formed; it gave a colourless solution in acetic acid. We did not study this product further.

Formal of 2-Hydroxymethyl-4-methyl-19-norcholesta-1,3,5(10)-trien-1-ol (VIII).—Fraction A (above) (2·4 g.) was chromatographed from alumina (100 g.); elution with hexane and hexane–benzene (95 : 5) yielded a crude product (0·45 g.), which crystallised successively from methanol and hexane, to give the *formal* (VIII) as needles, m. p. 132—134°, $[\alpha]_D$ +194°, $\lambda_{max.}$ 209 (ε 33,200), 228sh (ε 8800), 279 (ε 1870), and 287 mμ (ε 2090) (Found: C, 82·0; H, 10·15. $C_{29}H_{44}O_2$ requires C, 82·0; H, 10·4%).

Another method of making the formal is described below.

4-Dimethylaminomethylcholesta-1,4-dien-3-one (II).—Fraction B (above) (5·5 g.) in ethanol (20 ml.) was treated with anhydrous oxalic acid (1·13 g., reckoned as 1 equiv.) in ethanol (5 ml.). A white solid (4·45 g.), m. p. 200—202°, crystallised; several recrystallisations from ethanol or, better, propan-1-ol gave the pure *oxalate*, m. p. 210·5—212°, $[\alpha]_D$ +69°, $\lambda_{max.}$ 247 mμ (ε 15,200), $\nu_{max.}$ (Nujol) 1700, 1660, and 1600 cm.$^{-1}$ (Found: C, 72·3; H, 9·7; N, 3·0. $C_{32}H_{51}NO_5$ requires C, 72·5; H, 9·7; N, 2·65%), of base (II). This salt (0·50 g.) with ether and sodium carbonate afforded the oily base (II) (0·41 g.), $[\alpha]_D$ +57°, $\lambda_{max.}$ 241—242 mμ (ε 14,500), $\nu_{max.}$ 1660, 1628, 856, and 820 cm.$^{-1}$, in which form it was used in this work. It gave a *chloroplatinate*, m. p. 186—188° (from ethanol) (Found: C, 54·8; H, 8·2; N, 2·4; Pt, 15·0. $C_{60}H_{100}Cl_6N_2O_2Pt$ requires C, 55·9; H, 7·8; N, 2·2; Pt, 15·1%).

[15] Labat, *Bull. Soc. chim. France*, 1909, **5**, 745.
[16] Clemo, Haworth, and Walton, *J.*, 1930, 1110.
[17] Woodward and Singh, *J. Amer. Chem. Soc.*, 1950, **72**, 494.
[18] Burke, Barton, Gardner, and Lewis, *J. Amer. Chem. Soc.*, 1958, **80**, 3438.

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The base (II) was also obtained, in 8% yield, when the Mannich reaction was conducted for 65 hr. in refluxing isopentyl alcohol.

4α-Methyl-5α- (III) *and 4β-Methyl-5β-cholestan-3-one* (IV).—4-Dimethylaminomethylcholesta-1,4-dien-3-one (II) (0·83 g.), dissolved in benzene (30 ml.), was reduced with hydrogen over 2% palladium–charcoal (100 mg.). The reduction curve showed an inflection after absorption of *ca.* 1·3 mol. The reduction ended after the uptake of 3 mol. of hydrogen and gave a neutral wax (0·63 g., 84%), $[\alpha]_D$ +30°, which was chromatographed; elution with hexane–benzene (9 : 1) gave material that crystallised from methanol to give pure 4β-methyl-5β-cholestan-3-one (IV) (0·14 g., 19%), m. p. 55—57°, $[\alpha]_D$ +35°, $\nu_{max.}$ 1710 cm.$^{-1}$ (Found: C, 83·7; H, 11·7. Calc. for $C_{28}H_{48}O$: C, 83·9; H, 12·0%). Mixed m. p. and comparison of the infrared spectrum with an authentic specimen [10] kindly provided by Professor F. Sondheimer confirmed their identity. Later fractions from this column were combined, crystallised from methanol, and recrystallised from aqueous acetic acid, to give 4α-methyl-5α-cholestan-3-one (III) (0·176 g., 23%) as needles, m. p. 118·5—119·5°, $[\alpha]_D$ +27°, $\nu_{max.}$ 1712 cm.$^{-1}$ (Found: C, 83·9; H, 12·1%). Mixed m. p. and comparison of the infrared spectrum with an authentic specimen [9] kindly provided by Professor E. R. H. Jones confirmed their identity. The remainder of the neutral material was present in the intermediate fractions from the chromatographic separation. Previous workers [9,10] have shown that 4β-methyl-5α-cholestan-3-one, m. p. 125—127°, $[\alpha]_D$ +36°, is less easily eluted than the 4α-methyl isomer; consequently we carefully scanned the tail fractions from the column but found no evidence for the presence of a third isomer. The fourth isomer, 4α-methyl-5β-cholestan-3-one, has not been described. Optical rotatory dispersion curves of the isomers (III) and (IV) were in good agreement with published results.[19]

Hydrogenation of 4-Dimethylaminomethylcholesta-1,4-dien-3-one (II).—Reduction with Adams catalyst in glacial acetic acid at room temperature led to the uptake of 3 mol. of hydrogen in 45 min. The product was a basic, uncrystallisable foam, whose infrared spectrum showed the presence of a strongly bonded hydroxyl group ($\nu_{max.}$ 3230 cm.$^{-1}$). This product was not studied further.

Trimethyl-(3-oxocholesta-1,4-dien-4-yl)methylammonium Iodide (V).—The tertiary base (II) (0·32 g.) in dry ether (30 ml.) containing a few drops of absolute ethanol was treated with methyl iodide (1 ml.). The solution became cloudy and was refluxed for 1·5 hr. The *methiodide* (V) separated as a white precipitate (0·37 g.), m. p. 197—200°, $[\alpha]_D$ +46°, $\lambda_{max.}$ (in EtOH) 247·5 (ε 18,700), (in H_2O) 251 (ε 14,550) and 227 mμ (ε 18,750) (due to the iodide ion), $\nu_{max.}$ (in $CHBr_3$) 1660, 1626, and 1593 cm.$^{-1}$ (Found: C, 63·5; H, 9·0; N, 2·3; I, 21·6. $C_{31}H_{52}INO$ requires C, 64·0; H, 9·0; N, 2·4; I, 21·8%).

Attempts at the Hofmann Degradation of the Methiodide (V).—The methiodide (V) (0·45 g.) in water (30 ml.) was shaken overnight with freshly precipitated silver oxide (0·5 g.). Ether extracted a glass (21 mg.), softening at 80—85°, $[\alpha]_D$ +58°; the aqueous layer was boiled in a stream of nitrogen until the evolution of basic gases ceased. Ether then extracted a glass (135 mg.), softening 110—115°, $[\alpha]_D$ +63°, $\lambda_{max.}$ 237 mμ ($E^{1\%}_{1\,cm.}$ 222), infl. 269 mμ ($E^{1\%}_{1\,cm.}$ 101), $\nu_{max.}$ 1656, 1624, 830, and 800 cm.$^{-1}$. The infrared absorption at 830 and 800 cm.$^{-1}$ suggests the presence of triply substituted double bonds (cf. ref. 14). This substance resisted our attempts at purifying it.

In another experiment the methiodide (V) (1·0 g.) in water (300 ml.) was passed through a column of an Amberlite IR-4B ion-exchange resin (basic form) (20 g.). The eluates, which contained no halide ion, were refluxed for 2 hr., after which evolution of volatile bases was imperceptible. The *product* separated as a glassy precipitate (0·35 g.) of indefinite softening point, $[\alpha]_D$ +57°, $\lambda_{max.}$ 237 mμ ($E^{1\%}_{1\,cm.}$ 229), infl. 271 mμ ($E^{1\%}_{1\,cm.}$ 99), $\lambda_{min.}$ 218 mμ ($E^{1\%}_{1\,cm.}$ 160) [Found: *M* (Rast), 810. $C_{56}H_{84}O_2$ requires *M*, 789]. Sublimation at 10^{-4} mm. failed to effect a purification.

The product of the Hofmann degradation (117 mg.) in methylene dichloride (15 ml.) was subjected at −10° to a stream of ozone for 1·5 hr. at the rate of 0·5 mmole/min. Formaldehyde was identified as its dimedone derivative (13 mg.), m. p. and mixed m. p. 189°, in the volatile components of the reaction.

The Formal (VIII) *from 4-Methyl-19-norcholesta-1,3,5(10)-trien-1-ol* (VII).—A mixture of the phenol [12] (VII) (1·0 g.), dimethylamine hydrochloride (16 g.), and paraformaldehyde (12 g.) in acetic acid (200 ml.) was refluxed for 18 hr. The solvent was removed *in vacuo*, and the resulting oil shaken with ether and water. The ether phase was treated with aqueous sodium

[19] Djerassi, Halpern, Halpern, and Riniker, *J. Amer. Chem. Soc.*, 1958, **80**, 4001.

hydrogen carbonate; on evaporation it then yielded an oil (0·93 g.) that was chromatographed on alumina (30 g.; Grade O from Peter Spence and Sons Ltd., Widnes, Lancs.). Hexane eluted a fraction (0·36 g.) that yielded the formal (VIII) as white needles (from ethanol), m. p. 131—133°, $[\alpha]_D$ +193°, identified by mixed m. p. and absorption spectroscopy with the product obtained as described above from cholestadienone (I).

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GLAXO LABORATORIES LTD.,
GREENFORD, MIDDLESEX.

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586. *The Infrared Absorption of Normal and* ^{18}O*-Labelled* NN*-Dimethylbenzamide.*

By S. PINCHAS, DAVID SAMUEL, and MARTA WEISS-BRODAY.

The infrared absorption spectra of normal and 69 atom % ^{18}O-labelled *NN*-dimethylbenzamide in the 3700—670 cm.$^{-1}$ region were measured for carbon tetrachloride solutions and, where not possible, for Nujol mulls. The origins of the bands are discussed in relation to the shifts brought about by the isotopic substitution. Since the measured shift of 24 cm.$^{-1}$ in the tertiary amide C=O stretching frequency is equal to the corresponding shift of benzamide and its *N*-methyl derivative the " amide I " band of even the primary amides is a real C=O band.

The molecular extinction coefficient and relative integrated absorption intensity of the C=^{18}O band were found to be about 25% higher than the corresponding values for the C=^{16}O frequency, both for CCl_4 and for $CHCl_3$ solutions.

IT was shown recently that ^{18}O-labelled benzamide [1] and *N*-methylbenzamide [2] behave differently from the other substances studied which contain an X=^{18}O group [3] (X = C or P) by absorbing considerably more strongly (in CCl_4 solutions) than the corresponding normal compounds, at the X=O stretching frequency. It was thus of interest to investigate also the infrared absorption of the tertiary amides of this series *i.e.*, normal and labelled *NN*-dimethylbenzamide. The spectra of these compounds are also significant in interpretation of the characteristic amide bands. However, the infrared spectrum of even the unlabelled *NN*-dimethylbenzamide does not seem to have been reported. Samples of the normal and 68·7 atom % [^{18}O]-labelled *NN*-dimethylbenzamide were therefore synthesised and their infrared absorption bands were investigated (see Table 1 where the optical densities are in parentheses after the frequency).

The 3060 cm.$^{-1}$ band is due to the aromatic C–H stretching vibration; 2940 cm.$^{-1}$ is the asymmetrical methyl C–H stretching frequency: [4] normal *N*-methylbenzamide shows the methyl band at the same place.[2] The band that appears in the carbon tetrachloride solution spectrum of the normal amide at 1640 cm.$^{-1}$ and is shifted to 1616 cm.$^{-1}$ in the case of the ^{18}O-labelled compound is no doubt the C=O stretching band. The fact that this isotopic shift is the same as that for the analogous primary benzamide [1] and secondary *N*-methylbenzamide [2] (24 cm.$^{-1}$) shows again [2] that this " amide I " band is in practice a real C=O stretching absorption even though extensive coupling with an N–H bending or a

[1] Pinchas, Samuel, and Weiss-Broday, *J.*, 1961, 1688.
[2] Pinchas, Samuel, and Weiss-Broday, *J.*, in the press.
[3] Halmann and Pinchas, *J.*, 1958, (*a*) 1703, (*b*) 3264; (*c*) Pinchas, Samuel, and Weiss-Broday, *J.*, 1961, 2382.
[4] Jones and Sandorfy in " Technique of Organic Chemistry," Interscience Publ., Inc., New York, N.Y., 1956, Vol. IX, pp. 337, 392.

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C–N stretching mode of vibration is often suggested for it.[5,6] Since the tertiary *NN*-dimethylbenzamide does not contain an N–H group and its normal C=O and C–N bands (amide I and III bands, respectively) are at considerably different frequencies from, for instance, their positions in benzamide (in CCl_4: 1640 and about 1390 cm.$^{-1}$, compared

TABLE 1. *Absorption bands of normal and* ^{18}O*-labelled* NN*-dimethylbenzamide.*

Material	State	Concentration	Cell-thickness (mm.)	Bands (cm.$^{-1}$)
Normal	Solution	0·040 g. ± CCl_4 1 ml.	0·2	3060 (0·04), 2940 (0·18), ~1638 (>1), 1578 (0·22), 1504 (0·35), 1445 (0·36), 1388 (0·84), 1267 (0·34), 1214 (0·22), 1075 (0·47), 1027 (0·14), 927 (0·06)
69% ^{18}O	Solution	0·026 g. ± CCl_4 1 ml.	0·2	3060 (0·08), 2940 (0·18), ~1615 (>1), 1576 (0·20), 1504 (0·20), 1443 (0·22), 1389 (0·61), 1261 (0·18), 1215 (0·12), 1072 (0·33), 1027 (0·11), 927 (0·05)
Normal	Solution	9 g./l. in CCl_4	0·2	1640 (0·48) [a]
69% ^{18}O	Solution	10 g./l. in CCl_4	0·2	1616 (0·49) [a]
Normal	Solution	8 g./l. in $CHCl_3$	0·2	1622 (0·45) [a]
69% ^{18}O	Solution	8 g./l. in $CHCl_3$	0·2	1602 (0·44) [a]
Normal	Mull in Nujol [b]	—	Capillary	791, 733, 696, 673
69% ^{18}O	Mull in Nujol [b]	—	Capillary	789, 734, 696, 674

[a] Measured precisely and only in this region. [b] Measured only in the 830—670 cm.$^{-1}$ region (where CCl_4 is not transparent).

with [1] 1690 and 1358), one would expect that an appreciable coupling of N–H bending or C–N stretching with the C=O stretching in any (or all) of these amides to change the isotopic shift of the amide I band considerably from 24 cm.$^{-1}$.

The 1576/8 and 1504 cm.$^{-1}$ bands are probably due to the phenyl ring vibrations [7] of this region; the 1575/8 cm.$^{-1}$ band of *N*-methylbenzamide was assigned similarly.[2] The 1443/5 and 1388/9 cm.$^{-1}$ absorptions must be assigned to the asymmetrical and symmetrical methyl C–H bending vibrations, respectively. In *N*-methylbenzamide these vibrations bring about bands at 1484 and 1415 cm.$^{-1}$. The effect of the nitrogen atom, to which these methyl groups are bound, on their bending frequencies (causing them to shift from about [8] 1460 and 1380 cm.$^{-1}$) is, however, expected to be different in the *NN*-dimethylbenzamide case both because it is here split over two such groups and because the steric structure of this amide is different from that of *N*-methylbenzamide.[9] It is reasonable to assume that the very strong absorption at about 1390 cm.$^{-1}$ also includes the =C–N stretching band which appears in benzamide [1] at about 1360 cm.$^{-1}$ and should rise in frequency with methyl substitution on the nitrogen.[5]

The band which appears in the normal spectrum at 1267 cm.$^{-1}$ and is shifted by ^{18}O-labelling to 1261 cm.$^{-1}$ seems to be due to the asymmetrical C–CO–R stretching vibration, in analogy to the 1203 cm.$^{-1}$ band of benzoyl chloride,[3c] the 1250 cm.$^{-1}$ band of propionyl chloride,[10] and the 1200 cm.$^{-1}$ bands of ketones.[11] The material shift of 6 cm.$^{-1}$ because of ^{18}O-labelling strongly supports this assignment. A similar band also appears in the spectra of (melted) *NN*-diethylbenzamide [12] (at about 1280 cm.$^{-1}$), (liquid) *NN*-dimethylformamide [13] (at 1255 cm.$^{-1}$), *NN*-dimethylacetamide [12] (at about 1260 cm.$^{-1}$), and *NN*-diethylacetamide [12] (1270).

[5] Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1956, **24**, 408.
[6] Price and Fraser, *Proc. Roy. Soc.*, 1953, *B*, **141**, 66.
[7] Ref. 4, pp. 394—396.
[8] Ref. 4, p. 348.
[9] Edward and Meacock, *Chem. and Ind.*, 1955, 536.
[10] Nat. Acad. Sci., Nat. Bur. Standards, " Infrared Spectral Catalog," Compound Card No. 1687.
[11] Ref. 4, pp. 507—508.
[12] Lenormant, *Bull. Soc. chim. France*, 1948, **15**, 33.
[13] Cannon, British Nylon Spinners Collection, Documentation of Molecular Spectra Catalogue Compound Card No. 1001.

The absorption at about 1214 cm.$^{-1}$ seems to be connected with the relatively high intensity of the 1072/5 cm.$^{-1}$ band which amounts here to about 30% of the C=O band intensity while it is less than 10% in the case of *N*-methylbenzamide.[2] It appears reasonable to assume that these bands are due, to a large extent, to an asymmetrical and a symmetrical stretching vibration of the CH_3–N–CH_3 group, respectively. Colthup [14] also assigns two bands at about 1180 and 1080 cm.$^{-1}$ to tertiary amines; these bands are the result of the C–N stretching motions.[15] Dimethylformamide shows [13] similar bands at 1181 and 1094 cm.$^{-1}$. The band observed at about 1155 cm.$^{-1}$ in the spectra of *N*-methylacetamide [16] and *N*-methylbenzamide [2] can also be a C–N stretching [15] rather than an N–CH_3 rocking [16] band.

Part of the 1072/5 cm.$^{-1}$ absorption, as well as the 1027 cm.$^{-1}$ band, seems however to come from in-plane C–H bending frequencies of a monosubstituted benzene,[17] since *N*-methylbenzamide also shows such bands at [2] 1071 and 1030 cm.$^{-1}$.

The 927 cm.$^{-1}$ band is probably the result of the C_{ar}–CO stretching vibration, in analogy to the 935 cm.$^{-1}$ band of *N*-methylbenzamide.[2]

The bands observed with Nujol mulls of the isotopic *NN*-dimethylbenzamides at about 790, 696, and 673 cm.$^{-1}$ correspond to similar bands at about 802, 696, and 685 cm.$^{-1}$ in the spectrum of *N*-methylbenzamide which were assigned to aromatic C–H out-of-plane bending frequencies.[2] The additional absorption of the tertiary amides at 733/4 cm.$^{-1}$ may be the $(CH_3)_2$N-analogue of the $(CH_3)_2$CH-deformation band [18] at about 800 cm.$^{-1}$. Dimethylamine [19] also shows a (very intense) band at about 735 cm.$^{-1}$.

The value of 1640 cm.$^{-1}$ given in Table 1 for the C=O stretching band of normal *NN*-dimethylbenzamide, although somewhat lower than recently reported [20] (1644 cm.$^{-1}$) is in excellent agreement with the same value for this band in the case of *NN*-diethylbenzamide.[21] The published curve of the latter,[12] shows in the 5—8 μ region bands near 1650, 1530, 1470, 1440, 1380, 1315, and 1280 cm.$^{-1}$, similar to those of Table 1.

The Intensity of the Isotopic C=O *Bands.*—Optical-density measurements results for the C=O stretching bands of the normal and ^{18}O-labelled *NN*-dimethylbenzamide are collected in Table 2, with related results. It is evident that for *NN*-dimethylbenzamide, as for

TABLE 2. *Absorption intensity of the* C=O NN*-dimethylbenzamide bands.*

Materia	Solvent	Concn. (g./l.)	Cell-thickness (mm.)	Frequency (cm.$^{-1}$)	Optical density	Mol. extinction coeff. (l. mole^{-1} cm.$^{-1}$)	Apparent half-width (cm.$^{-1}$)	Integrated absorption (l. mole^{-1} cm.$^{-2}$)
Normal	CCl_4	8·95	0·2	1640	0·480	400 ± 6	22	8800 ± 400
Normal	CCl_4	8·35	0·2	1640	0·461	411 ± 19	23	9500 ± 500
69 atom % ^{18}O	CCl_4	10·0	0·2	1616	0·464 [a]	510 [b] ± 10	21 [c]	10,700 ± 300
69 atom % ^{18}O	CCl_4	11·3	0·2	1616	0·563 [a]	547 [b] ± 30	22 [c]	12,000 ± 1000
Normal	$CHCl_3$	7·55	0·2	1622	0·431	425 ± 16	28	11,900 ± 800
69 atom % ^{18}O	$CHCl_3$	7·7	0·2	1602	0·394 [a]	562 [b] ± 11	25·2 [c]	14,200 ± 300
69 atom % ^{18}O	$CHCl_3$	12·9	0·2	1602	0·664 [a]	565 [b] ± 20	24 [c]	13,600 ± 500

[a] Corr. for the absorption of the normal amide at this point. [b] Corr. for the lower effective concentration of the labelled amide. [c] Calc. after absorption of the normal amide had been subtracted.

benzamide [1] and *N*-methylbenzamide,[2] there is a considerable increase in the relative integrated absorption intensity of the C=^{18}O band. Thus the mean value for this intensity is 9100 ± 400 units for the normal amide in carbon tetrachloride solution but

[14] Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397.
[15] Ref. 4, p. 531.
[16] Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1958, **29**, 611.
[17] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen & Co. Ltd., London, 1958, pp. 81—82.
[18] Ref. 17, p. 27.
[19] Barr and Haszeldine, ref. 13, Compound Card No. 558.
[20] Schmulbach and Drago, *J. Phys. Chem.*, 1960, **64**, 1957.
[21] Ref. 4, p. 525.

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11,300 ± 700 units for the labelled amide (in CCl_4), an increase, due to the ^{18}O-labelling, of about 24%. It is remarkable that the corresponding values of the *N*-methylbenzamides are [2] 8900 ± 300 and 10,900 ± 300 units, and 22%. The values for the benzamides [1] are also in line, being 10,400 and 12,800 units, an increase of 23%.

The results for the chloroform solutions of the *NN*-dimethylbenzamides similarly show a marked increase in the absorption intensity of the ^{18}O-labelled modification (11,900 ± 800 to 13,900 ± 300). This behaviour of the tertiary amide is, however, different from that of benzamide [1] and *N*-methylbenzamide [2] the chloroform spectra of which do not show a significant change of intensity between the isotopic modifications (about 14,500 units with benzamides and about 12,000 with the *N*-methylbenzamides). It is also noteworthy that the width of the labelled tertiary amide CO band is as a rule lower than for the normal tertiary amide, while the opposite is true for the secondary benzamides.[2] The reason for these anomalies is unclear.

Ultraviolet Absorption.—*NN*-Dimethylbenzamide, when dissolved in propan-2-ol, showed (above 2200 Å) a single maximum of absorption at 2260 Å with a log ε of 3·83 (in ethanol, 3·87). The ^{18}O-labelled compound under identical conditions, however, showed a doublet at 2210 and 2280 Å with log ε 3·81 and 3·71 respectively. The reported absorption band of the normal compound [22] in methanol appears at 2250 Å (log ε 3·78). Lower ultraviolet absorption intensities (and a small change of the spectrum) as a result of exchanging an $X=^{16}O$ group for $X=^{18}O$ have been observed for [^{18}O]nitromethane and [^{18}O]benzophenone.[23] Methyl benzoate [3c] also shows differences in the intensity of its ultraviolet absorption as a result of ^{18}O-labelling.

Experimental

NN-*Dimethyl*[^{18}O]*benzamide.*—Dry dimethylamine was bubbled through [^{18}O]benzoyl chloride [3c] (2·5 g.) in dry ether, with cooling, to saturation. The precipitate was filtered off and washed repeatedly with dry ether. The combined filtrates were dried (Na_2SO_4) and evaporated to dryness. The *NN*-dimethylbenzamide (both portions), recrystallised from light petroleum, had m. p. 39—41° (Lieberman [24] gives m. p. 38—40° for the normal amide) (yield 90%). Care should be taken not to heat the amide at any stage above 30° to avoid difficulties in crystallisation. The product was analysed for its ^{18}O content as described by Samuel [25] and was found to contain 68·7 atom %. The normal amide was prepared in an analogous manner, and had the same m. p.

Infrared and ultraviolet absorption measurements were carried out as already described.[3c]

The Weizmann Institute of Science,
Rehovoth, Israel.

[*Received, February 7th*, 1961.]

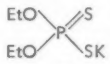
[22] Ley and Specker, *Ber.*, 1939, **72**, 199.
[23] Halmann and Pinchas, *J.*, 1960, 1246.
[24] Lieberman, *J. Amer. Chem. Soc.*, 1955, **77**, 1114.
[25] Samuel, *J.*, 1960, 1318.

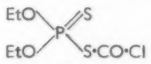
587. *The Reactivity of Organophosphorus Compounds. Part IV.*[1] *The Reaction of Carbonyl Chloride with Some Esters.*

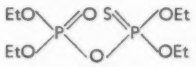
By J. I. G. Cadogan.

The reaction of carbonyl chloride with potassium *OO*-diethyl phosphorodithioate gives *S*-chlorocarbonyl *OO*-diethyl phosphorodithioate, a new type of organophosphorus compound, whereas potassium *OO*-diethyl phosphorothioate gives diethyl phosphorochloridate and tetraethyl pyrophosphoromonothionate. *S*-Ethyl methylphosphonochloridothioate, also a new type of organophosphorus compound, is readily obtained by reaction of carbonyl chloride with *OS*-diethyl methylphosphonothioate, whereas with the isomeric thionate loss of sulphur occurs to give ethyl methylphosphonochloridate.

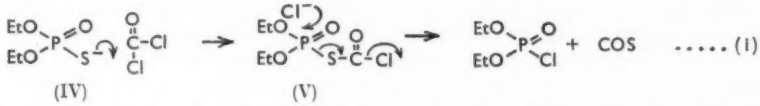
Although it is known that carbonyl chloride with dialkyl alkylphosphonates gives alkyl alkylphosphonochloridates [2] and with trialkyl phosphites gives dialkyl phosphorochloridates,[3] its reactions with organophosphorus compounds have generally received little attention. The reactions of other types of organophosphorus compound with carbonyl chloride have now been examined with a view to (*a*) the production of new types of compound or compounds difficult to prepare by other methods, and (*b*) the discovery of new facts likely to lead to the elucidation of the mechanisms of these reactions.


(I)


(II)


(III)

Potassium *OO*-diethyl phosphorodithioate (I) reacted readily with carbonyl chloride, to give *S*-chlorocarbonyl *OO*-diethyl phosphorodithioate (II), a new type of organophosphorus compound formed by nucleophilic displacement on carbonyl chloride. Attempts to characterise this compound by formation of the anilide failed, and *NN'*-diphenylurea, formed by successive displacements on the carbonyl carbon atom, was obtained. Potassium *OO*-diethyl phosphorothioate (cf. IV), on the other hand, gave a mixture of diethyl phosphorochloridate and tetraethyl pyrophosphoromonothionate (III), suggesting the intermediate formation of *S*-chlorocarbonyl diethyl phosphorothioate (V), followed by elimination of carbonyl sulphide by intramolecular decomposition or by bimolecular displacement by chloride ion (reaction i); the chloridate and unchanged potassium salt then give the pyrophosphorothionate (III). The instability of *S*-chlorocarbonyl diethyl phosphorothioate (V) compared with the dithioate (II) is presumably due to the increased electrophilicity of the phosphorus atom and parallels the higher reactivity of diethyl phosphorochloridate than of diethyl phosphorochloridothionate towards nucleophilic reagents.


(IV) (V) ..... (i)

Potassium *O*-ethyl methylphosphonothioate reacted similarly with carbonyl chloride, giving diethyl dimethylpyrophosphonomonothionate (VI). The absence of the corresponding chloridate in this case is in accord with its greater reactivity towards nucleophilic reagents. The presumed formation in the above reactions of the thiolo-isomer, *e.g.*, (V) rather than the isomeric thionate, *e.g.*, (VII) is noteworthy, since Kabachnik and his co-workers [4]

[1] Part III, Cadogan and Thomas, *J.*, 1960, 2248.
[2] Coe, Perry, and Brown, *J.*, 1957, 3604.
[3] Ford-Moore, Lermit, and Stratford, *J.*, 1953, 1776; Pudovik and Platanova, *J. Gen. Chem.* (*U.S.S.R.*), 1959, **29**, 507 (U.S. translation).
[4] Kabachnik, Mastryukova, Rodionova, and Popov, *Zhur. obshchei Khim.*, 1956, **26**, 120.

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report that *O*-acetyl *OO*-diethyl phosphorothioate results from the reaction of potassium *OO*-diethyl phosphorothioate and acetyl chloride, *i.e.*, C·O·P=S rather than C·S·P=O formation. Thus the behaviour of the bidentate ion (V) towards the carbonyl-carbon atom of carbonyl chloride is similar to its behaviour towards the α-carbon atom of an alkyl halide.[5] The carbonyl-carbon atom in methyl chloroformate, on the other hand, appears to be intermediate in character, because both C·O·P=S and C·S·P=O bond formation occur in its reaction with potassium *OO*-diethyl phosphorothioate. This observation apparently conflicts with that of Nesmeyanov and Kabachnik [6] who reported, but without experimental detail, the formation of the thiolo-isomer (VIII) rather than thionate in this reaction. In an earlier paper, however, Kabachnik and his co-workers [4] do not specify which isomer is formed. Our evidence is based on infrared absorptions which can be attributed to P·S·C, P·O·C, P=O, and P=S groups. The analogous reaction between methyl chloroformate and potassium *OO*-diethyl phosphorodithioate gave diethyl *S*-methoxycarbonyl phosphorodithioate (IX).

(VI) (VII) (VIII) (IX)

O-Ethyl *S*-propyl methylphosphonothioate (X; R = Pr^n) and diethyl methylphosphonothiolate (X; R = Et) on reaction with carbonyl chloride gave *S*-propyl (XI; R = Pr^n) and *S*-ethyl methylphosphonochloridothioate (XI; R = Et) respectively, providing a useful method for the preparation of these previously inaccessible compounds. Reaction of carbonyl chloride with diethyl methylphosphonothionate and with the dipropyl homologue, on the other hand, results in the loss of sulphur, presumably as carbonyl sulphide, to give ethyl and propyl methylphosphonochloridate. Triethyl phosphate, triethyl phosphorothionate, triethyl phosphorothiolate, and *OSS*-triethyl phosphorodithioate did not react with carbonyl chloride under the mild conditions employed in these investigations. It is difficult at this stage to arrive at a mechanism which embraces all of the observations made with neutral esters. That the unreactivity of the phosphates is due to the electronic

(X) (XI)

(XII) ..... (ii)

rather than steric effects, however, is clear from the ready reaction of the hindered diisopropyl propylphosphonate with carbonyl chloride. Mechanism (ii) is proposed for the reactions of carbonyl chloride with esters (XII) where Y = O and X = O or S, and where X = O and Y = S.

Experimental

The infrared spectra in the region 2—15 μ were obtained by using a Perkin–Elmer Model 21 double-beam spectrophotometer fitted with a rock-salt prism. Those in the region 15—25 μ were recorded on a Hilger H800 double-beam spectrophotometer fitted with a potassium bromide prism. Liquids were examined as capillary films between potassium bromide plates, and solids in potassium chloride or bromide discs. The provision of these facilities by Mr.

[5] Stirling, *J.*, 1957, 3597; Kabachnik, Mastryukova, Kurochkin, Rodionova, and Popov, *Zhur. obshchei Khim.*, 1956, **26**, 2228.
[6] Nesmeyanov and Kabachnik, *Experientia, Suppl.* II, 1955, 67.

L. C. Thomas, and his help in the interpretation of the spectra, which was in part based on his unpublished correlations, are gratefully acknowledged.

Triethyl phosphorothionate, prepared by the addition of sulphur to triethyl phosphite, had b. p. 96°/12 mm., n_D^{25} 1·4458. Triethyl phosphorothiolate [1] had b. p. 100°/12 mm., n_D^{25} 1·4565. Triethyl *OOS*-phosphorodithioate had n_D^{25} 1·5030. Diethyl methylphosphonothiolate, prepared from ethyl methylphosphonochloridate [2] and ethanethiol in the presence of triethylamine, had b. p. 90°/12 mm., n_D^{25} 1·4738. Potassium diethyl phosphorothioate, m. p. 197°, was prepared by Mastin's method.[7] *Potassium ethyl methylphosphonothioate*, m. p. 137—138° (sealed tube) (from ether–ethanol) (Found: C, 19·6; H, 4·7. $C_3H_8KO_2PS$ requires C, 20·2; H, 4·5%), was obtained as hygroscopic crystals by the hydrolysis of diethyl methylphosphonothionate by Mastin's method.[7] *O-Ethyl S-propyl methylphosphonothiolate* (50%), b. p. 106°/10 mm., n_D^{25} 1·4718 (Found: C, 39·7; H, 8·6. $C_6H_{15}O_2PS$ requires C, 39·5; H, 8·3%), was prepared by boiling diethyl methylphosphonothionate with an excess of propyl iodide for 92 hr.

Dipropyl methylphosphonothionate, prepared from sodium propoxide and methylphosphonothioic dichloride in propan-1-ol at room temperature (24 hr.), had b. p. 62—64°/0·03 mm., n_D^{23} 1·4603 (Found: C, 43·5; H, 8·7. $C_7H_{17}O_2PS$ requires C, 42·9; H, 8·8%).

Reaction of Carbonyl Chloride with Organophosphorus Esters.—(i) *With diethyl methylphosphonothiolate.* Dry (H_2SO_4) carbonyl chloride was bubbled through the ester for 12 hr. at room temperature in an apparatus protected by drying tubes (SiO_2 gel). The mixture was degassed by drawing dry air through it. Distillation of the residue gave *ethyl methylphosphonochloridothiolate* (75%), b. p. 46°/0·1 mm., n_D^{25} 1·5100 (Found: C, 23·1; H, 5·3. C_3H_8ClOPS requires C, 22·8; H, 5·05%). The infrared spectrum showed absorption at 8·15 (P=O), 7·7, 11·3 (P·Me [8]), and 18·7 μ (P·S·C [8]). The chloridate (1·71 g.) in benzene (3 ml.) was added to aniline (1·80 g.) in benzene (4·5 ml.) at 0°. After 30 min. the mixture was filtered and the residue (3·2 g.) was washed with water and filtered. The residue (2·0 g.) was recrystallised to constant m. p. (155°) from methanol–benzene, to give S-*ethyl* N-*phenylmethylphosphonamidothioate* in needles (Found: C, 50·3; H, 6·9. $C_9H_{14}NOPS$ requires C, 50·3; H, 6·5%). The infrared spectrum showed absorption at 8·55 (P=O), 3·2 (NH), 18·7 μ (P·S·C).

O-Ethyl *S*-propyl methylphosphonothioate was similarly treated with carbonyl chloride for 9 hr. and left overnight before being degassed; it gave *S*-propyl methylphosphonochloridothioate, n_D^{25} 1·4930. This was confirmed by conversion (75%) into S-*propyl* N-*phenylmethylphosphonamidothioate* which, on recrystallisation from benzene–light petroleum (b. p. 60—80°), had m. p. 98—100° (Found: C, 52·1; H, 7·2. $C_{10}H_{16}NOPS$ requires C, 52·5; H, 7·0%).

(ii) *With dialkyl methylphosphonothionates.* The diethyl ester (4·75 g.; n_D^{25} 1·4620) was treated with carbonyl chloride at room temperature for 3½ hr. during which the volume of the mixture had doubled. The product, after being degassed on the next day by passage of dry air, had n_D^{25} 1·4485. Treatment with carbonyl chloride was resumed for 1½ hr. and the next day degassing gave ethyl methylphosphonochloridate (4·0 g.), n_D^{25} 1·4374, having an infrared spectrum identical with that of authentic material. Coe, Perry, and Brown [2] reported n_D^{25} 1·4320.

The dipropyl ester (4·75 g.; b. p. 62—64°/0·03 mm., n_D^{23} 1·4603) was similarly treated but was kept for 3 days before excess of carbonyl chloride was removed; it gave propyl methylphosphonochloridate (3·0 g.), n_D^{20} 1·4350 (correct infrared spectrum). A portion (1·6 g.) of the chloridate on treatment with aniline (1·86 g.) gave propyl *N*-phenylmethylphosphonamidate (2·00 g.), b. p. 134°/0·05 mm. (Found: C, 55·6; H, 7·6. Calc. for $C_{10}H_{16}NO_2P$: C, 56·4; H, 7·5%).

(iii) *With di-isopropyl propylphosphonate.* Reaction with carbonyl chloride, which was vigorous at first, was allowed to proceed for 3 hr. The mixture was degassed on the next day to give isopropyl propylphosphonochloridate (80%), n_D^{23} 1·4310 (correct infrared spectrum).

(iv) *With potassium* OO-*diethyl phosphorodithioate.* The salt (20 g.) in light petroleum (b. p. 60—80°; 350 ml.; Na-dry) was stirred magnetically during the reaction, which was slow (by heat evolution), until the addition of dry ($MgSO_4$) acetone (50 ml.). The mixture was degassed after 3 hr., filtered, and evaporated at 20 mm. to leave an oil (19 g.), n_D^{25} 1·5130, which was distilled. This gave S-*chlorocarbonyl* OO-*diethyl phosphorodithioate*, b. p. 80°/0·05 mm., n_D^{25} 1·5198 (Found: C, 24·7; H, 3·9. $C_5H_{10}ClO_3PS_2$ requires C, 24·2; H, 4·0%). The infrared spectrum showed absorption at 12·05 (P=S [8]), 9·9, 10·25 [$(EtO)_2P$], 5·7 (C=O), 15·5 μ

[7] Mastin, *J. Amer. Chem. Soc.*, 1945, **67**, 1663.
[8] Thomas, *Chem. and Ind.*, 1957, 198.

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(~PS_2~ [9]). The product gave *NN'*-diphenylurea, m. p. and mixed m. p. 238°, on treatment with aniline (2 mol.).

(v) *With potassium* OO-*diethyl phosphorothioate*. The salt (15 g.) in light petroleum (b. p. 60—80°; 500 ml.; Na-dry), after reaction with carbonyl chloride (12 hr.), degassing, filtration, and evaporation (20 mm.), afforded an oil (12 g.), n_D^{25} 1·4628, which was not diethyl phosphorochloridate and had a spectrum similar to that of *S*-chlorocarbonyl *OO*-diethyl phosphorodithioate. The product was sealed in soda-glass to await purification by distillation, but decomposed violently after 4 days with the evolution of a gas. The experiment was repeated as follows: The salt (15 g.) was added during 10 min. to light petroleum (b. p. 60—80°; 150 ml.; Na-dry) which had been saturated with dry carbonyl chloride. Reaction occurred at once. The carbonyl chloride was passed through the magnetically stirred mixtured for 3 hr. The mixture was degassed on the next day, filtered, and evaporated at 20 mm. to leave an oil (5 g.), n_D^{23} 1·4570, which, on distillation at 0·05 mm. gave (*a*) diethyl phosphorochloridate, b. p. 40° (2 g.), n_D^{25} 1·4150 (correct infrared spectrum), and (*b*) tetraethyl pyrophosphoromonothionate, b. p. 90° (2·2 g.), n_D^{25} 1·4430 (infrared spectrum identical with that of authentic material [3]). Fraction (*a*) gave diethyl *N*-phenylphosphoramidate, m. p. and mixed m. p. 96°, on treatment with an excess of aniline. The unstable compound formed in the first experiment is therefore assumed to have been *S*-chlorocarbonyl diethyl phosphorothioate, which on decomposition would give diethyl phosphorochloridate, as discussed above.

(vi) *With potassium ethyl methylphosphonothioate*. The salt (15 g.) was added during 10 min. to light petroleum (b. p. 60—80°; 250 ml.) which had been saturated with carbonyl chloride. The reaction was very vigorous and required cooling; it was allowed to continue for 2 hr. After being degassed and filtered the solution was evaporated at 20 mm. to leave an oil (6 g.) which was distilled; this gave diethyl dimethylpyrophosphonomonothionate (4·9 g.), b. p. 80°/0·05 mm., n_D^{24} 1·4640. The infrared spectrum was identical with that of an authentic specimen. Coe, Perry, and Brown [2] reported b. p. 73°/3 × 10^{-4} mm., n_D^{20} 1·4679.

(vii) *With other esters*. The following esters did not react with carbonyl chloride at room temperature; the duration of reaction in hours is given in each case: triethyl phosphorothionate (18), triethyl phosphorothiolate (7), *OSS*-triethyl phosphorodithioate (12), triethyl phosphate (4 + overnight).

Reaction of Potassium OO-*Diethyl Phosphorodithioate with Methyl Chloroformate*.—The potassium salt (5·0 g.) and methyl chloroformate (2·6 g.) were boiled under reflux in ethyl methyl ketone (25 ml.) for 2 hr. Evaporation of the cooled, filtered mixture gave OO-*diethyl* S-*methoxycarbonyl phosphorodithioate* (5 g.), b. p. 80°/0·05 mm., n_D^{25} 1·5040 (Found: C, 30·2; H, 5·8. $C_6H_{13}O_4PS_2$ requires C, 29·6; H, 5·4%).

Reaction of Potassium OO-*Diethyl Phosphorothioate with Methyl Chloroformate*.—The reaction of the potassium salt (5·0 g.) with methyl chloroformate (2·4 g.), as described above, gave a colourless oil (4·0 g.), b. p. 86°/0·05 mm., n_D^{23} 1·4560 (Found: C, 32·6; H, 6·3. $C_6H_{13}O_5PS$ requires C, 31·6; H, 5·8%). The infrared spectrum showed bands at 9·8, 10·25 (P·O·Et), 7·9 (P=O), 12·25 (P=S), 17·85, 16·95 (P·S·C), and 5·65, 5·8 μ (C=O).

KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, December 21st*, 1960.]

[9] Thomas, 16th Internat. Congr., I.U.P.A.C., Paris, 1957, Resumé of Communications, Vol. II, p. 103.

588. *The Reactivity of Organophosphorus Compounds. Part V.*[1] *The Reaction of Trichloromethyl Radicals with Trialkyl Phosphites.*

By J. I. G. Cadogan and W. R. Foster.

From a knowledge of the reactions of benzyl and ββ-dimethylphenethyl radicals, evidence is produced in favour of the radical-induced reaction of carbon tetrachloride with trialkyl phosphites to give dialkyl trichloromethylphosphonates proceeding by a radical-chain reaction involving $[(RO)_3P{\cdot}CCl_3]^+Cl^-$ rather than by decomposition of the phosphoranyl radical $(RO)_3\dot{P}{\cdot}CCl_3$. Evidence concerning the reactivity of phosphoranyl radicals is presented and discussed.

Kamai and Egorava [2] first investigated the reaction between carbon tetrachloride and triethyl phosphite and isolated diethyl trichloromethylphosphonate (II; R = Et) and later [3] Kamai and Kharrasova described it as a radical-chain process. Griffin [4] confirmed the radical nature of this reaction and that with bromotrichloromethane by observing acceleration in the presence of dibenzoyl peroxide and ultraviolet light, findings which have been confirmed in this investigation. On this basis alternative reaction schemes can be formulated.

$$\text{(A)}\ \begin{cases} {\cdot}CCl_3 + (RO)_3P \longrightarrow (RO)_3\dot{P}{\cdot}CCl_3\ \text{(I)} \\ (RO)_3\dot{P}{\cdot}CCl_3 + CCl_4 \longrightarrow [(RO)_3P{\cdot}CCl_3]^+Cl^- + {\cdot}CCl_3 \\ [(RO)_3P{\cdot}CCl_3]^+Cl^- \longrightarrow (RO)_3P(O){\cdot}CCl_3\ \text{(II)} + RCl \end{cases}$$

$$\text{(B)}\ \begin{cases} {\cdot}CCl_3 + (RO)_3P \longrightarrow (RO)_3\dot{P}{\cdot}CCl_3 \longrightarrow (RO)_3P(O){\cdot}CCl_3\ \text{(II)} + R{\cdot} \\ R{\cdot} + CCl_4 \longrightarrow RCl + {\cdot}CCl_3 \end{cases}$$

Scheme A involves chain propagation by the reaction of the phosphoranyl radical (I) with carbon tetrachloride to give a phosphonium salt and a free trichloromethyl radical, the former then undergoing nucleophilic dealkylation to give the observed products and the latter continuing the chain by reaction with another molecule of trialkyl phosphite. Scheme B involves decomposition of the intermediate radical (I) into the trichloromethylphosphonate (II) and an alkyl radical which then continues the chain by attack on the solvent.

Unequivocal evidence in favour of either mechanism has hitherto been lacking. Griffin [4] favours scheme A but, as is admitted, without sufficient evidence. Walling and his co-workers,[5] on the other hand, support scheme B, largely by analogy with their work on a different reaction, that of trialkyl phosphites with thiols. For scheme B to be operative, it is essential that the radical R· should be capable of continuing the chain by attacking carbon tetrachloride. By suitable choice of the initial phosphite and thus of the radical R·, it was our intention to distinguish between the mechanisms.

It is well known [6] that the ββ-dimethylphenethyl radical, $Ph{\cdot}CMe_2{\cdot}CH_2{\cdot}$, when generated in solution, rearranges in part to the more stable αα-dimethylphenethyl radical, $Ph{\cdot}CH_2{\cdot}CMe_2{\cdot}$, and that both radicals can be detected by the products of their dimerisation and disproportionation, *i.e.*, $Ph{\cdot}CMe_3$, $Ph{\cdot}CH_2{\cdot}CHMe_2$, $Ph{\cdot}CH{:}CMe_2$, $Ph{\cdot}CH_2{\cdot}CMe{:}CH_2$, etc. Further, by analogy with related radicals, both radicals would be expected to attack carbon tetrachloride to give the corresponding chlorides. ββ-Dimethylphenethyl diethyl

[1] Part IV, Cadogan, preceding paper.
[2] Kamai and Egorava, *J. Gen. Chem.* (*U.S.S.R.*), 1946, **16**, 1521.
[3] Kamai and Kharrasova, *Zhur. obshchei Khim.*, 1957, **27**, 953.
[4] Griffin, *Chem. and Ind.*, 1958, 415; Amer. Chem. Soc. 135th Meeting, 1959, Abs., p. 690.
[5] Walling and Rabinowitz, *J. Amer. Chem. Soc.*, 1959, **81**, 1243; Walling, Basedow, and Savas, *ibid.*, 1960, **82**, 2181.
[6] Urry and Kharasch, *J. Amer. Chem. Soc.*, 1944, **66**, 1438; Winstein and Seubold, *ibid.*, 1947, **69**, 2916; Smith and Anderson, *ibid.*, 1960, **82**, 656.

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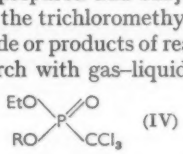
phosphite (III; R = Ph·CMe_2·CH_2·) has now been prepared and subjected to peroxide-catalysed reaction with carbon tetrachloride, to give the trichloromethylphosphonate (IV; R = Ph·CMe_2·CH_2). No ββ-dimethylphenethyl chloride or products of rearrangement of the derived radical were detected despite a rigorous search with gas–liquid chromatography.

(III) $(EtO)_2P{\cdot}OR$  (IV)

Strong evidence is thus presented in favour of scheme A. If the reaction had proceeded by way of scheme B, then elimination of both ethyl and ββ-dimethylphenethyl radicals would have probably occurred, since the energy requirements would be similar in each case. Scheme A involves nucleophilic attack (probably S_N2) on the alkyl group by chloride ion and it is known [7] that ββ-dimethylphenethyl compounds will not enter into such reactions whereas ethyl groups readily do; hence exclusive elimination of ethyl chloride, with retention of the dimethylphenethyl group in the phosphorus compound, as observed, is predictable on the basis of scheme A.

It was not found possible to obtain an analytically pure specimen of ethyl ββ-dimethylphenethyl trichloromethylphosphonate from the above reaction. Decomposition readily occurred on heating, to give a mixture (*ca.* 1 : 1) of 2-methyl-1- and 2-methyl-3-phenylpropene. This mixture was similar to that obtained by Heck and Winstein [7] on decomposition of ββ-dimethylphenethyl benzoate, which proceeded by way of the carbonium ion:

$$Ph{\cdot}CMe_2{\cdot}CH_2{}^+ \longrightarrow Ph{\cdot}CH_2{\cdot}CMe_2{}^+ \xrightarrow{Ph{\cdot}CO_2^-} Ph{\cdot}CH{:}CMe_2 + Ph{\cdot}CH_2{\cdot}CMe{:}CH_2$$

A similar mechanism probably operates in our reaction.

The results of the peroxide- and light-catalysed reaction of carbon tetrachloride with benzyl diethyl phosphite (III; R = Ph·CH_2·) can also be rationalised by scheme A which predicts, as a result of the extreme lability of benzyl groups towards halide ions,[8] exclusive debenzylation to give diethyl trichloromethylphosphonate (II; R = Et) and benzyl chloride, which were observed. Scheme B alternatively requires the elimination of resonance-stabilised benzyl radicals, some of which would be expected to dimerise to bibenzyl, which was not detected despite a careful search again by gas–liquid chromatography. Such dimerisation constitutes a chain-ending step and the reaction would therefore stop. In this case, however, it could be argued that scheme B was in fact operative and the benzyl radicals, formed exclusively because of the resultant resonance-stabilisation, had reacted entirely by abstraction of chlorine atoms rather than by dimerisation. That this was not the case is shown by the results of the decomposition of di-(9-benzyl-9-fluorenyl) peroxide in carbon tetrachloride and of di-t-butyl peroxide in a mixture of toluene and carbon tetrachloride. The former peroxide has recently been shown [9] to be a good source of free benzyl radicals, as is the decomposition of di-t-butyl peroxide in toluene.[10] These decompositions were carried out under conditions likely to give a concentration of benzyl radicals similar to that expected in the peroxide-catalysed reaction of carbon tetrachloride and benzyl diethyl phosphite if scheme B operates, and in each case benzyl chloride and bibenzyl were isolated. The absence of bibenzyl from the products of the reaction with benzyl diethyl phosphite therefore supports scheme A. It is noteworthy that benzyl chloride is formed in the reactions of di-(9-benzyl-9-fluorenyl) peroxide and of di-t-butyl peroxide and toluene in carbon tetrachloride, thus showing that a benzyl radical will abstract chlorine from carbon tetrachloride, which is at variance with the conclusions of Kharasch, Kane, and Brown [11] and of Leffler and Bartlett.[12]

[7] Heck and Winstein, *J. Amer. Chem. Soc.*, 1957, **79**, 3432.
[8] Clarke and Todd, *J.*, 1950, 2030.
[9] Cadogan, Hey, and Sanderson, *J.*, 1960, 3203.
[10] Beckwith and Waters, *J.*, 1957, 1001; Farmer and Moore, *J.*, 1951, 131.
[11] Kharasch, Kane, and Brown, *J. Amer. Chem. Soc.*, 1942, **64**, 1622.
[12] Bartlett and Leffler, *J. Amer. Chem. Soc.*, 1950, **72**, 3030.

It is therefore concluded that the free-radical-induced reaction of carbon tetrachloride with trialkyl phosphites proceeds by a radical-chain mechanism involving $[(RO)_3P{\cdot}CCl_3]^+Cl^-$ rather than by decomposition of the phosphoranyl radical $(RO)_3\dot{P}{\cdot}CCl_3$. This is contrary to the suggestion of Walling *et al.*[5] who have proposed the following mechanism for the formation of trialkyl phosphorothionates in the reaction of trialkyl phosphites with thiols:

$$(C)\begin{cases}(RO)_3P + R'S\cdot \longrightarrow (RO)_3\dot{P}{\cdot}SR' \longrightarrow (RO)_3PS + R'\cdot \\ R'\cdot + R'SH \longrightarrow R'H + R'S\cdot\end{cases}$$

This mechanism corresponds to scheme B above, which Walling favours for the reaction of carbon tetrachloride and trialkyl phosphites. It is now clear that different mechanisms operate in the reactions of phosphites with trichloromethyl radicals on the one hand and with thiyl radicals on the other. This is clearly a function of the properties of the two possible phosphoranyl radicals $(RO)_3\dot{P}{\cdot}CCl_3$ and $(RO)_3\dot{P}{\cdot}SR$. It could be argued that the thiophosphoranyl radical was intrinsically less stable than the trichloromethylphosphoranyl radical, thus providing a rationalisation of the difference. That this cannot be so follows from the results of the reaction, initiated by dibenzoyl peroxide, of triethyl phosphite with an equimolar mixture of carbon tetrachloride and butane-1-thiol, which gives diethyl trichloromethylphosphonate (22%), triethyl phosphorothionate (18%), and *S*-butyl diethyl phosphorothioate (60%). The formation of the first two products can be explained on the basis of simultaneous operation of schemes A and C. Much more significant is the formation of the thiolate, which indicates that the thiophosphoranyl radical can also behave like the trichloromethylphosphoranyl radical by readily abstracting a chlorine atom from carbon tetrachloride as follows:

$$(EtO)_3P + Bu^nS\cdot \longrightarrow (EtO)_3\dot{P}{\cdot}SBu^n$$
$$(EtO)_3\dot{P}{\cdot}SBu^n + CCl_4 \longrightarrow [(EtO)_3P{\cdot}SBu^n]^+Cl^- + \cdot CCl_3$$
$$[(EtO)_3P{\cdot}SBu^n]^+Cl^- \longrightarrow (EtO)_3P(O){\cdot}SBu^n + EtCl$$

The thiophosphoranyl radical can also therefore behave according to scheme A, and incidentally provides a new method of preparation of phosphorothiolates. The possibility that the trichloromethylphosphoranyl radical might also react by scheme B under circumstances depending on a suitable choice of substituents cannot be entirely discounted, however, as a result of these experiments.

The propensity of a phosphoranyl radical to abstract a chlorine atom, and thus to react by way of an Arbuzov-type intermediate (scheme A), is probably a result of the favourable energetics of formation of this intermediate. On the other hand, abstraction of a hydrogen atom would presumably give rise to an unstable compound, so decomposition of the phosphoranyl radical is the favoured process. This reluctance to abstract hydrogen is further exemplified by the radical-induced reaction[4] of chloroform with triethyl phosphite to give diethyl dichloromethylphosphonate, thus:

$$\cdot CHCl_2 + (EtO)_3P \longrightarrow (EtO)_3\dot{P}{\cdot}CHCl_2$$
$$(EtO)_3\dot{P}{\cdot}CHCl_2 + CHCl_3 \longrightarrow [(EtO)_3P{\cdot}CHCl_2]^+Cl^- + \cdot CHCl_2 \longrightarrow (EtO)_2P(O){\cdot}CHCl_2 + EtCl$$

whereas it is established[13] that radical-abstraction of hydrogen is usually the preferred reaction, the greater resonance energy of the trichloromethyl radical formed apparently overcoming the greater strength of the C–H bond involved. It is therefore clear that scheme A also obtains in the reaction of chloroform with triethyl phosphite, because scheme B calls for attack on chloroform by an ethyl radical which would extract *hydrogen* to give first a trichloromethyl radical and then diethyl trichloromethylphosphonate instead of the observed dichloromethyl compound.

Finally, it should be noted that the above discussion of mechanism is pertinent only

[13] Hey and Peters, *J.*, 1960, 79; Walling, "Free Radicals in Solution," Wiley & Sons, 1957, p. 255.

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to the cases where peroxide and light initiation is known to occur, since experiments with purified triethyl phosphite and carbon tetrachloride in darkened flasks show that formation of diethyl trichloromethylphosphonate is appreciably fast in the absence of peroxidic initiators at 80°, although not as fast as the reaction induced by dibenzoyl peroxide or ultraviolet light. In the former case the possibility that the peroxide is being partially removed in an ionic reaction with phosphite is a complication which cannot be ignored, however.

Experimental

Gas–liquid chromatography was carried out with a Perkin–Elmer "Fraktometer," model 116, fitted with a high-sensitivity dual thermal-conductivity detector which normally gives a response proportional to molecular weight. This response was tested wherever possible by analysis of mixtures of known composition and was satisfactory.

Benzyl diethyl phosphite, prepared by the method of Hoffman, Ess, and Usinger,[14] who reported b. p. 85—88°/1 mm., n_D^{25} 1·4905, had b. p. 70°/0·1 mm., n_D^{25} 1·4900 (Found: C, 57·9; H, 7·2. Calc. for $C_{11}H_{17}O_3P$: C, 57·9; H, 7·5%).

Preparation of ββ-Dimethylphenethyl Diethyl Phosphite.—ββ-Dimethylphenethyl chloride, b. p. 101°/12 mm., n_D^{21} 1·5241, prepared by the method of Smith and Sellas,[15] who reported b. p. 97—98°/10 mm., n_D^{20} 1·5250, was converted into the alcohol as follows: oxygen was passed (3 hr.) through a solution in ether of the Grignard reagent from ββ-dimethylphenethyl chloride (250 g.) at 0°. The mixture was poured into dilute sulphuric acid (2 l.), and the ether solution was washed with water and dried ($MgSO_4$). Distillation gave the alcohol, b. p. 110—112°/12 mm., n_D^{24} 1·5248 (102 g.). The infrared spectrum showed the absence of the chloride. Whitmore, Weisberger, and Shabica [16] reported b. p. 131°/30 mm., n_D^{20} 1·5261.

The alcohol (25 g.) and triethyl phosphite (56·5 g., 1 mol.) were kept at 140° for 4½ hr. and the ethanol (80%) formed was removed through a still-head. The residue, on distillation (twice), gave *ββ-dimethylphenethyl diethyl phosphite* (27 g., 61%), b. p. 98—102°/0·1 mm., n_D^{25} 1·4892 (Found: C, 62·3; H, 8·9. $C_{16}H_{23}O_3P$ requires C, 62·3; H, 8·6%).

Attempts to prepare tris-(ββ-dimethylphenethyl) phosphite by standard reactions gave oils which readily decomposed when heated.

Reaction of Benzyl Diethyl Phosphite with Carbon Tetrachloride in the Presence of Dibenzoyl Peroxide.—Benzyl diethyl phosphite (5·3 g.) and dibenzoyl peroxide (0·3 g., 0·05 mol.) in carbon tetrachloride (15 g.) were boiled under reflux for 18 hr. After removal of the solvent the residue was distilled at 13 mm., giving fractions: (*a*) benzyl chloride, b. p. 40—80°, $n_D^{23\cdot5}$ 1·5240 (1·5 g.), identified by comparison of infrared spectrum and of gas–liquid chromatographic retention time with those of authentic material, (*b*) b. p. 80—90°, $n_D^{23\cdot5}$ 1·5070 (0·8 g.), (*c*) b. p. 90—110°, $n_D^{23\cdot5}$ 1·4770 (0·95 g.), and (*d*) diethyl trichloromethylphosphonate, b. p. 120—130°, $n_D^{23\cdot5}$ 1·4620 (4·2 g.), identified by comparison of infrared spectrum and gas–liquid chromatographic retention time with those of authentic material prepared as described below. Fractions (*b*) and (*c*) were similarly shown to be mixtures of benzyl chloride and diethyl trichloromethylphosphonate. The ester formed 28% of fraction (*b*) and 75% of fraction (*c*). Thus were obtained benzyl chloride (0·86 mol.) and diethyl trichloromethylphosphonate (0·83 mol.). Gas–liquid chromatography of the product before the distillation showed the absence of bibenzyl.

Reaction of ββ-Dimethylphenethyl Diethyl Phosphite with Carbon Tetrachloride in the Presence of Dibenzoyl Peroxide.—Dibenzoyl peroxide (0·44 g.) and the ester (10 g.) in carbon tetrachloride (24 g.) were boiled under reflux for 18 hr. After removal of the solvent, the residue was shown by gas–liquid chromatography to contain no ββ-dimethylphenethyl chloride. A portion (50%) of the residue was distilled at 12 mm., decomposition occurring and giving an unsaturated oil, b. p. 90—105°/12 mm., n_D^{20} 1·5208 (2·8 g.), ε 7499 at 244 mμ. Heck and Winstein [7] obtained a product having almost identical properties (n_D^{25} 1·5208, ε 6912 at 244 mμ) from the unimolecular decomposition of ββ-dimethylphenethyl benzoate which proceeded by way of the carbonium ion, and was identified as an equimolar mixture of 2-methyl-1- (n_D^{25} 1·5364; ε 14,000 at 244 mμ) and 2-methyl-3-phenylpropene (n_D^{25} 1·5057; ε 77). The infrared spectrum of our

[14] Hoffmann, Ess, and Usinger, *J. Amer. Chem. Soc.*, 1956, **78**, 5817.
[15] Smith and Sellas, *Org. Synth.*, 1952, **32**, 90.
[16] Whitmore, Weisberger, and Shabica, *J. Amer. Chem. Soc.*, 1943, **65**, 1469.

product was compatible with a mixture of this type, the composition of which was calculated from a refractive index plot (2-methyl-1-phenylpropene, 53%) and from the absorption at 244 mμ (same ingredient, 56%). This was further confirmed by hydrogenation, the amount of hydrogen corresponding to such a mixture being taken up.

Distillation of a further portion of the residue was attempted at 10^{-4} mm. It gave an oil, b. p. 110°, n_D^{24} 1·5080. Some decomposition occurred even under these conditions and the product is formulated as impure ββ-dimethylphenethyl ethyl trichloromethylphosphonate (Found: C, 47·5; H, 5·5. Calc. for $C_{13}H_{18}Cl_3O_3P$: C, 43·5; H, 5·0%).

Reaction of Triethyl Phosphite with Carbon Tetrachloride.—(i) *In the presence of dibenzoyl peroxide.* Triethyl phosphite (5 g.) and the peroxide (0·05 mol.) in carbon tetrachloride (15 g.) were boiled under reflux for 18 hr. Distillation gave diethyl trichloromethylphosphonate (6·85 g., b. p. 128°/14 mm., n_D^{20} 1·4620. Griffin [4] reported b. p. 137—138°/17 mm., n_D^{20} 1·4612.

(ii) *In the absence of peroxide.* In a similar experiment, in which was used carbon tetrachloride that had been passed through alumina to remove any peroxidic material, the reaction was carried out in the dark and without dibenzoyl peroxide. Diethyl trichloromethylphosphonate (6·94 g., n_D^{25} 1·4597, was again formed.

Triphenyl phosphite did not react with carbon tetrachloride or bromotrichloromethane under either of the above sets of conditions.

Rate of Disappearance of Triethyl Phosphite in its Reactions with Carbon Tetrachloride.—The rate of disappearance of triethyl phosphite on reaction with carbon tetrachloride at 80° was determined by following the reaction by gas–liquid chromatography. Portions (1 ml.) of a standard solution of the ester (8·35 g.) in carbon tetrachloride (24·5 ml.) were immersed in sealed tubes in a thermostat at 80°, removed at intervals (10 min.), and immersed in an ice–salt bath. The amounts of triethyl phosphite remaining were determined by chromatography. The first-order rate constant was found to be $2·2 \times 10^{-4}$ sec.$^{-1}$.

The experiment was repeated in the presence of added dibenzoyl peroxide (0·05 mol.), the rate constant being $3·5 \times 10^{-4}$ sec.$^{-1}$.

Reaction of Triethyl Phosphite with Carbon Tetrachloride in Ultraviolet Light.—A mixture of the phosphite (5 ml.) and carbon tetrachloride (15 ml.) was degassed by bubbling nitrogen through the solution and then irradiated in a quartz flask under nitrogen from an "Hanovia" source ($\lambda_{min.}$ 2500 Å) at room temperature for 1 hr. Distillation gave diethyl trichloromethylphosphonate (70%).

Triethyl phosphite and carbon tetrachloride had not reacted after 7 hr. in the dark at room temperature.

Decomposition of Di-t-butyl Peroxide in Toluene in the Presence of Carbon Tetrachloride.—Di-t-butyl peroxide (3·7 g.) in toluene (18·4 g.) and carbon tetrachloride (31·1 g.) was heated in a sealed tube at 130° for 48 hr. After removal of the solvents distillation gave fractions (*a*) b. p. 50—85°/13 mm. (2·8 g.) and (*b*) b. p. 50—75°/0·1 mm. (1·2 g.). Fraction (*a*) was shown by gas–liquid chromatography to be largely benzyl chloride (0·66 mole per mole of peroxide) together with an unidentified component. Fraction (*b*) was similarly shown to be bibenzyl (0·12 mol.) with the same unidentified component. Treatment of fraction (*b*) with light petroleum (b. p. 40—60°) gave bibenzyl, m. p. and mixed m. p. 48—50°. The unidentified component may be 2,2,2-trichloroethylbenzene.

Decomposition of Di-(9-benzyl-9-fluorenyl) Peroxide in Carbon Tetrachloride.—The peroxide (0·5 g.), m. p. 170—170·5°, prepared as described by Cadogan, Hey, and Sanderson,[9] was heated in carbon tetrachloride (2·2 ml.) and benzene (2 ml.) in a sealed tube at 130° for 48 hr. After removal of the solvents the residue was examined by gas–liquid chromatography. Bibenzyl and benzyl chloride (0·25 : 1 mol.) were identified by comparison with authentic mixtures. Also present was the unidentified compound found in the previous experiment.

Dibenzoyl Peroxide-initiated Reaction of Triethyl Phosphite with Carbon Tetrachloride and Butane-1-thiol.—A mixture of triethyl phosphite (8·3 g., 0·05 mol.), carbon tetrachloride (15·4 g., 0·1 mol.), butane-1-thiol (9·0 g., 0·1 mol.), and dibenzoyl peroxide (0·61 g., 0·0025 mol.) was refluxed overnight. After removal of the solvents the residue (10·8 g.) was analysed by gas–liquid chromatography in a 1-m. column packed with "Apiezon L" on Celite (545). With a column temperature of 166°, the following components, with relative retention times given in parentheses, were identified by comparison with mixtures of known composition: triethyl phosphorothionate (18%; 1·00), diethyl trichloromethylphosphonate (22%; 2·95), and *S*-butyl diethyl phosphorothioate (60%; 5·29).

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Reaction of Benzyl Diethyl Phosphite and Carbon Tetrachloride in Ultraviolet Light.—Irradiation of the phosphite (3·18 g.) in carbon tetrachloride (15 ml.) under nitrogen at room temperature for 4 hr., followed by fractionation, gave benzyl chloride (0·70 g.), b. p. 90°/17 mm., n_D^{25} 1·4995, and diethyl trichloromethylphosphonate (1·27 g.), b. p. 110°/17 mm., n_D^{25} 1·4670, and left a residue (1·8 g.). The nature of these products was confirmed by infrared spectroscopy.

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KING'S COLLEGE, STRAND,
LONDON, W.C.2.

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589. *The Reactivity of Organophosphorus Compounds. Part VI.*[1] N-*Chloroamidates.*

By J. I. G. CADOGAN and W. R. FOSTER.

Various *N*-chloro-phosphor- and -phosphon-amidates, representatives of a new class of organophosphorus compounds, have been prepared. *N*-Aryl-*N*-chloro-derivatives have been shown to rearrange under heterolytic (Orton-type) and homolytic conditions to give nuclear chlorinated products. Ratios of isomerides and rates of rearrangement have been measured in some cases.

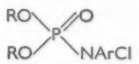
ALTHOUGH *N*-aryl-*N*-chloro-amides are well known in carbon chemistry, no reports of corresponding *N*-chloro-derivatives of phosphorus amides have appeared. Audrieth, Zimmer, and Zimmer's recent report [2] that they had failed to prepare such compounds leads us to describe the preparation and properties of various phosphorus *N*-chloroamides which we have recently investigated.

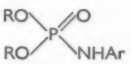
N-Aryl-*N*-chlorophosphoramidates such as diphenyl *N*-chloro-*N*-phenylphosphoramidate (I; R = Ar = Ph) are easily prepared by the reaction of t-butyl hypochlorite with the corresponding phosphoramidate in a methanolic solution of borax, a method used to convert acetanilide into *N*-chloroacetanilide.[3] *N*-Aryl-*N*-chlorophosphoramidates undergo the usual rearrangements in acid solution [4] to give nuclear-chlorinated derivatives, *e.g.*, diphenyl *N*-chloro-*N*-phenylphosphoramidate (I; R = Ar = Ph) rearranged in acetic acid in the presence of hydrochloric acid to a mixture of isomeric diphenyl *N*-chlorophenylphosphoramidates (II; R = Ph, Ar = C_6H_4Cl). The ratio of isomerides [*o*/(*m* + *p*)] was determined in this and other cases by acid-hydrolysis to isomeric chloroanilines, which were analysed by gas–liquid chromatography. In this case the ratio was that expected from heterolytic chlorination. Similar results were obtained on rearrangement of diethyl *N*-chloro-*N*-phenylphosphoramidate (I; R = Et; Ar = Ph) in acetic–hydrochloric acid. The rearrangement of diphenyl *N*-chloro-*N*-phenylphosphoramidate (I; R = Ar = Ph) in acetic–hydrochloric acid in the presence of diphenyl *N*-*p*-tolylphosphoramidate (II; R = Ph; Ar = *p*-C_6H_4Me) was also carried out: hydrolysis of the product and analysis of the substituted anilines indicated the presence of chloro-*p*-toluidines (15%), showing intermolecular chlorination here, as in the carboxamide series.

Homolytic rearrangements of the *N*-chlorophosphoramidates have also been shown to occur readily. Irradiation with white light of a benzene solution of diethyl *N*-chloro-*N*-phenylphosphoramidate (I; R = Et, Ar = Ph), or reaction of this amidate with a catalytic amount of dibenzoyl peroxide in bromobenzene, led to homolytic chlorination of the nucleus, as revealed by the high (50%) yield of *o*-chloroaniline produced on acid hydrolysis. The large amount of *ortho*-substitution recalls the correspondingly high figure for

[1] Part V, Cadogan and Foster, preceding paper.
[2] Audrieth, Zimmer, and Zimmer, *J. prakt. Chem.*, 1959, **8**, 117.
[3] Chusty and Israelstam, *J. S. African Chem. Inst.*, 1956, **9**, 30.
[4] See Beard and Hickinbottom, *J.*, 1958, 2982.

benzene derivatives with free aryl radicals.[5] The ratio of isomerides (50% of *ortho*) produced by rearrangement of this amidate in boiling acetic acid indicates that homolytic chlorination occurs in this case also, even in the absence of free-radical initiators.


(I)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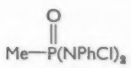
(III)

The rates of rearrangement, induced by dibenzoyl peroxide, of diphenyl (I; R = Ar = Ph) and diethyl (I; R = Et; Ar = Ph) *N*-chloro-*N*-phenylphosphoramidate in bromobenzene were also measured. As expected, no significant differences were noted, but the rate contours showed autocatalytic characteristics, as in similar experiments with *N*-chloroacetanilide and related compounds.[6] The rearrangements in the acetanilide series appear to be considerably slower than those of the phosphoramidates. Qualitative observations indicated that *N*-aryl-*N*-chlorophosphoramidates were relatively stable on storage in daylight, *ca.* 3 or 4 days being needed for complete rearrangement. The compound believed to be *NN'*-dichloro-*P*-methyl-*NN'*-diphenylphosphonodiamidate (III), formed from the corresponding amidate, on the other hand, rearranged so rapidly that it could not be isolated.

Experimental

Gas–liquid chromatography was carried out as described in Part V.[1]

Preparation of Amidates.—t-Butyl hypochlorite was prepared by the method of Teeter *et al.*[7] The following amidates were prepared by inter-reaction of the appropriate chloridate and amine. Recorded values for m. p.s are given in parentheses; diethyl *N*-phenylphosphoramidate, m. p. 96° (96·5° [8]); diphenyl *N*-phenylphosphoramidate, m. p. 129—130° (128—129° [9]); diphenyl *N*-*p*-tolylphosphoramidate, m. p. 135° (134° [10]); ethyl *NN'*-diphenylphosphorodiamidate, m. p. 114·5° (114° [11]); *P*-ethyl-*NN'*-diphenylphosphonodiamidate, m. p. 147° (147° [12]); *ethyl* P-*ethyl*-N-*phenylphosphonamidate*, pale yellow, b. p. 134°/0·05 mm., m. p. 32° (Found: C, 56·1; H, 7·6. $C_{10}H_{16}NO_3P$ requires C, 56·3; H, 7·5%); diethyl *N*-*p*-chlorophenylphosphoramidate, m. p. 73° (76° [13]); 1-diphenoxyphosphinylpiperidine, m. p. 74·5° (70° [11]); diphenyl phosphoramidate, m. p. 150—152° (148—149° [9]); diethyl phosphoramidate, m. p. 52° (50—51° [14]); diphenyl *N*-cyclohexylphosphoramidate, m. p. 101—102° (101—102° [9]).

Preparation of N-*Chloroamidates.*—The method is exemplified by the following preparation of diphenyl *N*-chloro-*N*-phenylphosphoramidate. t-Butyl hypochlorite (5·25 g., 6 ml.) was added to diphenyl *N*-phenylphosphoramidate (11·0 g.) in 4% methanolic borax (200 ml.). After 5 min. the mixture was poured into water (1 l.), and the oil which separated was extracted with chloroform. The extracts were washed with water and dried ($MgSO_4$). Evaporation at 20 mm. left an almost colourless solid which on recrystallisation from light petroleum (b. p. 40—60°) gave colourless *diphenyl* N-*chloro*-N-*phenylphosphoramidate* (9 g.), m. p. 63·5—64·5° (Found: Active Cl, 10·5. $C_{18}H_{15}ClNO_3P$ requires Cl, 10·85%).

The following *N*-chloroamidates were similarly prepared: *Diethyl* N-*chloro*-N-*phenylphosphoramidate*, a yellow liquid (92%), n_D^{25} 1·5089 (Found: Active Cl, 13·0. $C_{10}H_{15}ClNO_3P$ requires Cl, 13·5%), which decomposed on storage to a solid from which was isolated diethyl *N*-*p*-chlorophenylphosphoramidate, m. p. and mixed m. p. 70°; the chloroamidate is 40% decomposed after 48 hr. at 25°. *Diphenyl* N-*chloro*-N-p-*tolylphosphoramidate*, yellow (95%), m. p. 62—63° (Found: Active Cl, 9·1. $C_{19}H_{17}ClNOP$ requires Cl, 9·5%). *Diethyl* N-*chloro*-p-*chlorophenylphosphoramidate*, a yellow liquid (96%), n_D^{25} 1·5170 (Found: Active Cl, 11·5.

[5] Augood and Williams, *Chem. Rev.*, 1957, **57**, 123.
[6] Ayad, Beard, Garwood, and Hickinbottom, *J.*, 1957, 2981.
[7] Teeter, Bachmann, Bell, and Cowan, *Ind. Eng. Chem.*, 1949, **41**, 849.
[8] Foster, Overend, and Stacey, *J.*, 1951, 980.
[9] McCombie, Saunders, and Stacey, *J.*, 1945, 380.
[10] Michaelis and Schulze, *Ber.*, 1894, **27**, 2572.
[11] Michaelis, *Annalen*, 1903, **326**, 129.
[12] Cadogan, *J.*, 1957, 1079.
[13] Otto, *Ber.*, 1895, **28**, 613.
[14] Atherton, Openshaw, and Todd, *J.*, 1945, 660.

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$C_{10}H_{14}Cl_2NO_3P$ requires 1Cl, 11·9%). *Ethyl* N-*chloro*-P-*ethyl*-N-*phenylphosphonamidate*, yellow liquid (93%), n_D^{25} 1·5164 (Found: Active Cl, 13·6. $C_{10}H_{15}ClNO_2P$ requires Cl, 14·3%), which slowly decomposed at room temperature (n_D^{25} 1·5207 after 3 hr.). *Diphenyl* N-*chloro*-N-*cyclohexylphosphoramidate*, a colourless liquid (98%), n_D^{16} 1·5508 (Found: Active Cl, 8·3. $C_{18}H_{21}ClNO_3P$ requires Cl, 9·7%), that is unstable (20% purity after 48 hr.) and was prepared in subdued light.

Attempts to prepare these compounds by reaction of t-butyl hypochlorite in the absence of borax but in ether or benzene gave impure products. Attempts to prepare pure samples of ethyl *NN'*-dichloro-*NN'*-diphenylphosphorodiamidate and *NN'*-dichloro-*P*-ethyl-*NN'*-diphenylphosphonodiamidate failed, due to their extreme instability; diphenyl phosphoramidate was recovered from the reaction mixture, but tars were also formed.

Rearrangement of Diphenyl N-*Chloro*-N-*phenylphosphoramidate*.—(i) *In acetic acid*. The *N*-chloroamidate (1 g.) in acetic acid (25 ml.) was boiled under reflux for 48 hr. The mixture was poured into water (100 ml.), and the product extracted in methylene chloride and dried ($MgSO_4$). Evaporation left an oil which on treatment with light petroleum (b. p. 40—60°) gave diphenyl *N*-*p*-chlorophenylphosphoramidate (0·25 g.) with m. p. and mixed m. p. 116° and the correct infrared spectrum.

(ii) *In acetic–hydrochloric acid*. The *N*-chloroamidate (3 g.) in acetic acid (20 ml.) was treated with 10N-hydrochloric acid (6 drops). The reaction was complete after 4 min. (starch–iodide paper). After neutralisation with solid sodium carbonate and addition of water (20 ml.) crude diphenyl *N*-*p*-chlorophenylphosphoramidate (2·8 g.; m. p. 90—104°, mixed m. p. 110°) separated. Hydrolysis of this product with boiling 4N-hydrochloric acid for 1½ hr. gave a mixture of monochloroanilines (90%).

Comparison of the gas–liquid chromatogram of this mixture with that of authentic mixtures showed its composition to be *o*-chloroaniline (13·5 ± 1%) and *m*- and *p*-chloroanilines (86·5 ± 1%). The *meta*- and *para*-isomers could not be resolved.

(iii) *In benzene under the influence of light*. The *N*-chloroamidate (3 g.) in benzene (25 ml.) was irradiated by white light (Crompton Spotlight; 150 w) for 72 hr. at room temperature. The excess of benzene was removed by distillation, the last traces being examined by gas–liquid chromatography for the presence of chlorobenzene. Only benzene was detected. The residual oil, on treatment with light petroleum (b. p. 40—60°), gave diphenyl *N*-*p*-chlorophenylphosphoramidate, m. p. 100—105°. Recrystallisation from benzene–light petroleum (b. p. 60—80°) gave the pure product (0·4 g.), m. p. and mixed m. p. 116—117°. Repetition of the experiment with subsequent acid-hydrolysis of the residual oil, as described above, gave a mixture of anilines (*o*-chloroaniline 53%; *m*- and *p*-chloroaniline 46%; aniline *ca.* 2%).

Rearrangements of Other N-*Chloroamidates*.—*Diethyl* N-*chloro*-N-*phenylphosphoramidate*. Rearrangements as described above gave the following results: acetic–hydrochloric acid gave a mixture of diethyl chlorophenyl-amidates, from which was isolated the *para*-isomer (m. p. and mixed m. p. 72°). Hydrolysis gave *o*-chloroaniline (18%) and *m*- + *p*-chloroaniline (82%). Rearrangement of the *N*-chloroamidate in boiling acetic acid followed by acid-hydrolysis gave *o*-chloroaniline (50%) and *m*- + *p*-chloroaniline (50%). Irradiation by white light gave a similar mixture, from a portion of which was isolated diethyl *p*-chlorophenylphosphoramidate (m. p. and mixed m. p. 71—73°); hydrolysis of another portion gave *o*-chloroaniline (54%), *m*- + *p*-isomers (46%). Similar results (49, 51%) were obtained in a reaction catalysed by dibenzoyl peroxide in bromobenzene at 105°.

(ii) *Diethyl* N-*chloro*-N-p-*chlorophenylphosphoramidate*. Rearrangement of the amidate (1·3 g.) in acetic–hydrochloric acid gave *diethyl* N-2,4-*dichlorophenylphosphoramidate* (0·5 g.), m. p. 62—63° [from light petroleum (b. p. 60—80°)] (Found: C, 40·7; H, 4·79; N, 4·4; Cl, 30·0%; *M*, 257. $C_{10}H_{14}Cl_2NOP$ requires C, 40·3; H, 4·7; N, 4·70; Cl, 23·85%; *M*, 266). Hydrolysis of the amidate by 4N-hydrochloric acid gave 2,4-dichloroaniline, m. p. and mixed m. p. 58—59° (benzoyl derivative, m. p. and mixed m. p. 117°). Michaelis,[11] however, reported m. p. 105° for this 2,4-dichlorophenylphosphoramidate.

(iii) *Ethyl* N-*chloro*-P-*ethyl*-N-*phenylphosphonamidate*. Rearrangement in acetic–hydrochloric acid, followed by acid-hydrolysis, gave *o*-chloroaniline 17% and *m*- + *p*-chloroaniline 83%.

(iv) *Diphenyl* N-*chloro*-N-*phenylphosphoramidate in the presence of diphenyl* N-p-*tolyl-phosphoramidate*. Rearrangement of this *N*-chloroamidate in the presence of diphenyl *N*-*p*-tolylphosphoramidate (1 mol.) in acetic–hydrochloric acid followed by acid-hydrolysis gave a

mixture of amines: *p*-toluidine + *o*-chloroaniline 31·5%, *m*- + *p*-chloroanilines 36·5%, 2-chloro-4-methylaniline + 3-chloro-4-methylaniline 15%, aniline 17%.

Rates of Rearrangement of N-*Chloroamidates.*—Dibenzoyl peroxide (0·05 mol.) was added to a 0·1M-solution of the *N*-chloroamidate in bromobenzene at 105°. Aliquot parts (10 ml.) were removed at intervals and dissolved in acetic acid and the amounts of positive chlorine were determined iodometrically. Control experiments were also carried out. Because the reactions were autocatalytic, first-order rate constants were calculated from the initial slopes of the curves. Diphenyl *N*-chloro-*N*-phenylphosphoramidate had $10^4k = 1·5$ ($\pm 0·5$) sec.$^{-1}$; diethyl *N*-chloro-*N*-phenylphosphoramidate had $10^4k = 2·0$ ($\pm 0·5$) sec.$^{-1}$.

KING'S COLLEGE, STRAND,
LONDON, W.C.2.

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590. *The Reactivity of Organophosphorus Compounds. Part VII.*[1] *Reactions between Phosphites and Chloramine-*T.

By J. I. G. CADOGAN and H. N. MOULDEN.

Dialkyl hydrogen phosphites react with aqueous chloramine-T to give dialkyl hydrogen phosphates. Triethyl and triphenyl phosphites similarly give the corresponding phosphates.

VARIOUS reagents have been employed with varying success for the oxidation of phosphites to the corresponding phosphates. In many cases, particularly with the triesters, the oxidation is accompanied by side reactions and poor yields of the required product are obtained.

Air or oxygen has been used with triesters and in some cases the methods have been moderately successful.[2,3] Triesters have also been oxidised by such agents as hydrogen peroxide,[4] oxides of nitrogen,[5] and epoxides.[6] Alkaline potassium permanganate appears to be a good reagent for the oxidation of monoalkyl and dialkyl phosphites,[7] and Dimroth and Ploch [7a] obtained high yields of 2-chloroethyl dihydrogen phosphate and di-(2-chloroethyl) hydrogen phosphate from the corresponding phosphites. This reagent, however, is of little use for the preparation of trialkyl phosphates, which were obtained in yields ranging between 10 and 40%. Anhydrous chlorination or bromination, followed by mild hydrolysis, has been used to convert dialkyl hydrogen phosphites into the corresponding phosphates. This method is successful for the preparation of dibenzyl hydrogen phosphate.[8-10] Free halogens,[9] sulphuryl chloride,[8,11] *N*-chlorosuccinimide, and *N*,2,4-trichloroacetanilide [10] have been used as halogenating agents. These methods cannot be applied to convert trialkyl phosphites into trialkyl phosphates since the former, on reaction with chlorine [12] and sulphuryl chloride [13] give dialkyl phosphorochloridates. The reaction between triaryl phosphites and halogens has been studied by Rydon and Tonge.[14] The

[1] Part VI, Cadogan and Foster, preceding paper.
[2] Kuznetsov and Valetdinov, *Trudy Kazan. Khim. Teknol. Inst. im S.M. Kirova*, 1956, **21**, 167; *Chem. Abs.*, 1957, **51**, 11,985 f.
[3] Kamai and Koshkina, *Trudy Kazan. Khim. Teknol. Inst.*, 1953, **17**, 11 (*Referat. Zhur. khim.*, 1955, No. 526; *Chem. Abs.*, 1956, **50**, 6346 i).
[4] Stetter and Steinacker, *Ber.*, 1952, **85**, 451.
[5] Cox and Westheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5441; Kuhn, Doali, and Wellman, *ibid.*, 1960, **82**, 4792.
[6] Scott, *J. Org. Chem.*, 1957, **22**, 1118.
[7] (*a*) Dimroth and Ploch, *Ber.*, 1957, **90**, 801; (*b*) Brown and Hammond, *J.*, 1960, 4229.
[8] Atherton, Howard, and Todd, *J.*, 1948, 1106.
[9] Atherton, Openshaw, and Todd, *J.*, 1945, 382.
[10] Kenner, Todd, and Weymouth, *J.*, 1952, 3675.
[11] Miyano, *J. Amer. Chem. Soc.*, 1955, **77**, 3524.
[12] McCombie, Saunders, and Stacey, *J.*, 1945, 380.
[13] Poshkus and Herweh, *J. Amer. Chem. Soc.*, 1957, **79**, 6127.
[14] Rydon and Tonge, *J.*, 1956, 3043.

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reactions are complex and the products, on hydrolysis, give the corresponding triaryl phosphates, phenols, phosphoric acid, and primary and secondary aryl phosphates.

The reactions of chloramine-T and phosphites are now reported. Chloramine-T with triethyl phosphite in boiling aqueous ethanol gives triethyl phosphate (90%) and toluene-*p*-sulphonamide. Triphenyl phosphite and chloramine-T, in water, similarly give triphenyl phosphate in 69% yield. The lower yield is thought to be due to the method of its separation from the other reaction products. These reactions are thought to involve the formation of intermediate cations of the type $[(RO)_3PCl]^+$, which are then hydrolysed to the phosphate. The formation of intermediate compounds richer in chlorine can be discounted for two reasons. First, it was found that triethyl phosphite required only one molecular proportion of chloramine-T for almost complete oxidation. Secondly, Rydon and Tonge [14] have indicated that compounds such as $(PhO)_3PCl_2$ on hydrolysis give phenol and diphenyl hydrogen phosphate whereas only traces of these compounds were detected in the products of the oxidation of triphenyl phosphate. Kirsanov and Shevchenko [15] have reported the formation of triaryl *N*-arylsulphonylphosphorimidates (I; Ar = Ph, R = Ar) by the reaction of anhydrous chloramine-B and triaryl phosphites, and it was thought possible that these compounds were intermediates in the aqueous oxidations. This possibility is discounted since we did not isolate triethyl phosphate from the reaction between aqueous chloramine-T and the triethyl ester (I; Ar = *p*-Me·C_6H_4, R = Et). Instead, impure diethyl *N*-toluene-*p*-sulphonylphosphoramidate (II; R = Et), inorganic phosphate, and toluene-*p*-sulphonamide were isolated.

Triethyl *N*-toluene-*p*-sulphonylphosphorimidate (I; Ar = *p*-Me·C_6H_4, R = Et) was synthesised by allowing anhydrous chloramine-T to react with triethyl phosphite in dry carbon tetrachloride, and its identity was confirmed by comparison with a sample prepared from sodium ethoxide and *N*-toluene-*p*-sulphonylphosphorimidic trichloride (III). A small quantity of diphenyl *N*-toluene-*p*-sulphonylphosphoramidate (II; R = Ph) was isolated from the reaction of triphenyl phosphite and aqueous chloramine-T. Thus, in this reaction it is probable that the phosphorimidate (I; Ar = *p*-Me·C_6H_4, R = Ph) is formed to a slight extent and is subsequently hydrolysed to the phosphoramidate (II; R = Ph) and phenol, a trace of which was detected in the products. Kirsanov and Shevchenko [16] found that the phosphorimidates (I) on hydrolysis gave the phosphoramidates of type (II).

$ArSO_2{\cdot}N{=}P(OR)_3$	$p\text{-Me}{\cdot}C_6H_4{\cdot}SO_2{\cdot}NH{\cdot}P(O)(OR)_2$	$p\text{-Me}{\cdot}C_6H_4{\cdot}SO_2{\cdot}N{=}PCl_3$
(I)	(II)	(III)

Dialkyl hydrogen phosphites with aqueous chloramine-T give the corresponding dialkyl hydrogen phosphates. Diethyl and di-n-propyl hydrogen phosphates were obtained in yields of 90 and 80%, respectively. The yield of dimethyl hydrogen phosphate was much lower, probably because of hydrolysis. The reaction probably involves the formation of the dialkyl phosphorochloridate, by way of the phosphonate form, which is then hydrolysed, but attempts to isolate diethyl phosphorochloridate from the reaction with diethyl hydrogen phosphite were unsuccessful. Continuous ether extraction of the acidified reaction mixture, after the removal of the toluene-*p*-sulphonamide, was found to be the best method of isolating the dialkyl hydrogen phosphates.

Experimental

Triethyl phosphite (b. p. 52°/12 mm., n_D^{25} 1·4114) was fractionally distilled before use. Triphenyl phosphite was purified by fractional freezing. Examination of its infrared spectrum showed it not to contain phosphate. Anhydrous chloramine-T was prepared by dehydrating the trihydrate with phosphorus pentoxide at 70°/0·1 mm. Extracts were dried over magnesium sulphate and the light petroleum used had b. p. 40—60°. M. p.s are corrected.

Reaction with Aqueous Chloramine-T.—(a) *Triethyl phosphite.* Triethyl phosphite (3·97 g.)

[15] Kirsanov and Shevchenko, *J. Gen. Chem. U.S.S.R.*, 1956, **26**, 75.
[16] Kirsanov and Shevchenko, *J. Gen. Chem. U.S.S.R.*, 1954, **24**, 1980, 483.

and chloramine-T (6·75 g.), in 60% aqueous ethanol (120 ml.), were boiled under reflux for 11 hr. under an atmosphere of carbon dioxide. Ethanol was distilled from the solution, and the residue was allowed to cool. Toluene-*p*-sulphonamide (3·47 g.), m. p. and mixed m. p. 138—139°, was collected and washed with light petroleum. Chloroform extracts of the filtrate, combined with the light-petroleum washings, gave triethyl phosphate (3·97 g.), b. p. 50—54°/14 mm., n_D^{25} 1·4032 (which was identified by its infrared spectrum), and more toluene-*p*-sulphonamide (0·38 g.).

(b) *Triphenyl phosphite.* Triphenyl phosphite (5·0 g.) and chloramine-T (4·55 g.), in water (130 ml.), were boiled under reflux with stirring for 3 hr. Ether washings of the condenser gave a small quantity of impure phenol (0·02 g.) (odour and infrared spectrum). On cooling, the reaction mixture was basified (Na_2CO_3) and then extracted with ether. The ether extracts were evaporated and the residue was extracted with benzene, leaving toluene-*p*-sulphonamide (1·07 g.), m. p. and mixed m. p. 138°. The benzene extracts were evaporated and the residue adsorbed on neutral alumina. Elution with benzene (500 ml.) gave triphenyl phosphate (3·65 g.), m. p. 44—48°, which was identified by its infrared spectrum; and then with ether (500 ml.) to give toluene-*p*-sulphonamide (0·36 g.), m. p. and mixed m. p. 139°. Subsequent elution with ethanol (1500 ml.) gave the *aluminium diphenyl* N-*toluene*-p-*sulphonylphosphoramidate* (0·6 g.), m. p. 178—179° on crystallisation from ethanol–light petroleum (Found: S, 7·4. $C_{57}H_{51}AlN_3O_{15}P_3S_3$ requires S, 7·8%). It was dissolved in water and treated with hydrochloric acid. Crystallisation of the precipitate from benzene–light petroleum afforded *diphenyl* N-*toluene*-p-*sulphonylphosphoramidate*, m. p. 188—190° undepressed by admixture with a specimen described below. The original aqueous layer was acidified (hydrochloric acid) and then neutralised (sodium hydrogen carbonate). Chloroform extracts gave toluene-*p*-sulphonamide (0·41 g.), m. p. 131—136° not depressed by admixture with authentic material. The aqueous layer was acidified (hydrochloric acid) and extracted with chloroform to give a brown oil (0·34 g.) which, from its infrared spectrum, was considered to be impure diphenyl hydrogen phosphate.

(c) *Diethyl hydrogen phosphite.* Diethyl hydrogen phosphite (3·45 g.) was added to chloramine-T (7·05 g.), in water (50 ml.). The mixture became warm and a solid was precipitated. The mixture was gently warmed to 80° until no reaction was observed with starch–iodide test papers (*ca.* 20 min.). The reaction mixture was made alkaline (sodium carbonate) and extracted continuously with ether (16 hr.). The ether extracts gave toluene-*p*-sulphonamide (40 g.), m. p. and mixed m. p. 138—139°, on recrystallisation from water. The aqueous layer was acidified (hydrochloric acid) and extracted continuously with ether (24 hr.) to give diethyl hydrogen phosphate (3·51 g.), which was identified by its infrared spectrum [Found: equiv. (by titration), 158. Calc. for $C_4H_{11}O_4P$: equiv., 154].

The experiment was repeated and the reactants were mixed at 5°. The mixture, which became warm, was set aside for 2 min. and then extracted with chloroform. The extracts were dried immediately and then distilled. No diethyl phosphorochloridate was isolated.

In preliminary experiments it was found that prolonged heating of the acidic solution, after the oxidation was complete, produced hydrolysis of the product.

(d) *Dimethyl hydrogen phosphite.* Dimethyl hydrogen phosphite (2·75 g.) and chloramine-T (7·05 g.), in water (50 ml.), were boiled under reflux until reaction was complete. Toluene-*p*-sulphonamide (4·30 g.) and dimethyl hydrogen phosphate (1·28 g.) were isolated as described above (Found: equiv., 129. Calc. for $C_2H_7O_4P$: equiv., 126).

(e) *Di-isopropyl hydrogen phosphite.* Di-isopropyl hydrogen phosphite (4·15 g.) and chloramine-T (7·05 g.), in water (50 ml.), were boiled under reflux until reaction was complete. Toluene-*p*-sulphonamide (4·26 g.) and di-isopropyl hydrogen phosphate (3·62 g.) were isolated as described (Found: equiv., 189. Calc. for $C_6H_{15}O_4P$: equiv., 182).

Triethyl N-*Toluene*-p-*sulphonylphosphorimidate.*—Triethyl phosphite (10·0 g.) in dry carbon tetrachloride (100 ml.) was added slowly to anhydrous chloramine-T (11·40 g.), also in dry carbon tetrachloride, and the mixture boiled for 1 hr. After being washed with water, the organic layer was distilled to give unchanged phosphite (3·33 g.), b. p. 50—69°/14 mm., and the phosphorimidate (13·3 g.), b. p. 159—170°/0·01 mm., n_D^{25} 1·5041, whose identity was confirmed by comparison of its infrared spectrum with that of a specimen (n_D^{25} 1·5038) prepared by Kirsanov and Shevchenko's method [16] from *N*-toluene-*p*-sulphonylphosphorimidic trichloride and sodium ethoxide (Found: C, 47·0; H, 6·8; N, 4·2. Calc. for $C_{13}H_{22}NO_5PS$: C, 46·6; H, 6·6; N, 4·2%).

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Reaction with aqueous chloramine-T. The above phosphorimidate (5·0 g.) and chloroamine-T (4·21 g.), in water (50 ml.), were boiled for 22 hr. during which time the pH of the mixture changed from 8 to 2. The mixture was made alkaline (sodium carbonate) and extracted continuously with ether (16 hr.). The ether extracts gave a semi-solid which was heated at 90—100°/0·5 mm. for 1 hr. Nothing distilled into a receiver which was cooled in ice. The semi-solid was crystallised from benzene giving toluene-*p*-sulphonamide (0·67 g.), m. p. 134—135°. The mother liquors were fractionally precipitated with light petroleum into five fractions. Spectroscopic examination showed that the first fraction was impure sulphonamide and that the remaining fractions were mixtures of unchanged phosphorimidate and toluene-*p*-sulphonamide. The original aqueous layer was acidified (hydrochloric acid) and extracted continuously with ether (16 hr.). The ether extracts gave an oil (1·19 g.) which was identified as diethyl *N*-toluene-*p*-sulphonylphosphoramidate by comparison of its infrared spectrum with that of authentic material prepared, by Ratz's method,[17] from diethyl phosphorochloridate and sodium toluene-*p*-sulphonamide.

*Diphenyl N-Toluene-*p*-sulphonylphosphoramidate.*—Anhydrous chloramine-T and triphenyl phosphite gave *triphenyl N-toluene-*p*-sulphonylphosphorimidate*, m. p. 72—75° (aqueous ethanol), by the method described above (Found: C, 62·9; H, 4·5. $C_{25}H_{22}NO_5PS$ requires C, 62·65; H, 4·6%). Hydrolysis of the phosphorimidate with 0·4N-aqueous ethanolic sodium hydroxide [16] gave diphenyl *N*-toluene-*p*-sulphonylphosphoramidate, m. p. 186—187·5°, from benzene–light petroleum (Found: C, 56·3; H, 4·6. $C_{19}H_{18}NO_5PS$ requires C, 56·65; H, 4·5%).

Messrs. Albright and Wilson Ltd. are thanked for gifts of chemicals.

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[17] Ratz, *J. Org. Chem.*, 1957, **22**, 372.

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591. *The Pyrolysis of Methyl Nitrite.*

By L. PHILLIPS.

The pyrolysis of methyl nitrite at temperatures between 150° and 240° has been investigated and the products have been analysed. The initial step is O–N bond fission to form methoxyl radicals and nitric oxide, which above ~180° react to form nitroxyl and formaldehyde, the former ultimately giving nitrous oxide and water. The effects of the products and of added hydrogen-donors in relation to the formation of nitrous oxide have been studied. Reaction of ethoxyl radicals with methyl nitrite and [$^2H_3$]methyl nitrite shows that hydrogen-abstraction is slow compared with disproportionation of alkoxyl. A kinetic analysis which accounts for all the major experimental facts has been developed. The effect of added nitric oxide on the pyrolysis of ethyl nitrite has been re-examined and an earlier report that production of nitrous oxide then increased was not confirmed.

As a result of early work by Steacie and Shaw [1] it is usually assumed that alkyl nitrites undergo O–N bond fission on pyrolysis at 200—250°, affording alkoxyl radicals and nitric oxide, the former being converted into alcohols and aldehydes or ketones. Doubt was cast on this simple mechanism by Carter and Travers [2] who found that some nitrous oxide was formed. More recently, Levy [3] showed that, in the pyrolysis of ethyl nitrite, extensive reduction of initially formed nitric oxide to nitrous oxide occurs, and he invoked the reactions:

$$Me{\cdot}CH_2{\cdot}O{\cdot} + NO \longrightarrow HNO + Me{\cdot}CHO$$

$$2HNO \longrightarrow N_2O + H_2O$$

[1] Steacie and Shaw, *Proc. Roy. Soc.*, 1934, *A*, **146**, 388.
[2] Carter and Travers, *Proc. Roy. Soc.*, 1937, *A*, **158**, 495.
[3] Levy, *J. Amer. Chem. Soc.*, 1956, **78**, 1780.

Arden and Powling [4] studied product-composition profiles in the decomposition flame from methyl nitrite at atmospheric pressure and found almost no reduction to nitrous oxide in the first stage of the flame, suggesting that under these conditions no nitroxyl (HNO) was formed from methoxyl and nitric oxide. Gray and Williams [5] have, however, recently reported that, under flow conditions simulating the decomposition flame, appreciable reduction to nitrous oxide occurs. Shaw and Trotman-Dickenson [6] have also reported that the pyrolysis is more complex than was originally thought.

The following work, carried out in 1957—1959, concerns the various reactions in the pyrolysis of methyl nitrite, which was studied in more detail than hitherto, and enables a fairly complete picture of the mechanism to be drawn.

Experimental

Materials.—Methyl nitrite was initially prepared from methanol and nitrous acid by Gray and Style's method,[7] condensed at −80°, fractionated *in vacuo*, and stored in blackened flasks. In later work the simple exchange between methanol and pentyl nitrite was used. Infrared spectra showed that both products were identical. Ethyl nitrite was prepared by the latter method.

[$^2H_3$]Methyl nitrite was prepared by exchange between [$^2H_4$]methanol (Merck) and pentyl nitrite. Purification was as for methyl nitrite.

Dimethyl peroxide was prepared by Rieche's method.[8] Diethyl peroxide was prepared by hot ethylation of hydrogen peroxide with diethyl sulphate.[9]

Cyclohexene was free from peroxides by shaking it with aqueous ferrous sulphate, then dried and distilled, the fraction boiling at 82—83° being used.

Other substances used were prepared by conventional methods.

Pyrolysis.—Pyrolysis was carried out recently in a conventional static apparatus, including a Pyrex reaction vessel (144 c.c.) fitted with a Pyrex spiral gauge manometer and mirror. The electrically heated furnace was controlled to ±0·1° with a Sunvic RT 2 resistance-thermometer controller. The original analytical scheme involved freezing reaction products in a liquid-nitrogen trap, warming the latter, and sharing the products with an infrared cell at ambient temperature. This method failed because (*a*) polymerisation of formaldehyde occurred, (*b*) formaldehyde hemiacetal, which was formed in the trap, did not completely dissociate into formaldehyde and methanol when warmed and complicated the infrared spectra, and (*c*) results for nitric oxide and unchanged methyl nitrite were inconsistent owing to hydrolysis of the nitrite by the water formed. The method finally adopted, which removed these difficulties, was to expand the hot products into an infrared cell at 120°, as used by Arden and Powling,[4] connecting tubing being electrically heated to about 100° to prevent polymerisation of formaldehyde. The following infrared absorption bands (μ) were used: formaldehyde 3·68, 5·74; methanol 9·68; nitrous oxide 4·5; nitric oxide 5·25; methyl nitrite 12·335; formaldoxime 11·24; hydrogen cyanide 14·05. Allowance was made for the methyl nitrite overlap at 9·68 when estimating methanol. Carbon monoxide and nitric oxide were also estimated mass-spectrometrically after fractionation. Water was estimated by the Fischer method, after removal of volatile material at −50°. The accuracy of the analytical methods was checked against known mixtures.

The flow apparatus used was of the conventional type, inlet and exit reactor pressures being measured with modified oil–mercury magnification manometers (20/1).[10] Products passed through two liquid-oxygen traps which retained all except carbon monoxide, hydrogen, and nitric oxide; these three were pumped into a storage flask and analysed for mass-spectrometrically for nitric oxide; the other products, after warming, were analysed by infrared spectrometry.

[4] Arden and Powling, *Combustion and Flame*, 1958, **2**, 55.
[5] Gray and Williams, *Nature*, 1960, **188**, 56.
[6] Shaw and Trotman-Dickenson, *J.*, 1960, 3210.
[7] Gray and Style, *Trans. Faraday Soc.*, 1952, **48**, 1137.
[8] Rieche, *Ber.*, 1928, **61**, 951.
[9] Wiley, U.S.P. 2,357,298.
[10] Drucker, Jiméno, and Kangro, *Z. phys. Chem.*, 1915, *A*, **90**, 513.

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Results and Discussion

Pressure–time curves at 190—244° showed a first-order reaction to about 85% completion, in agreement with Steacie and Shaw's results,[1] and rate constants calculated from them and from loss of nitrite were in good agreement. Product analysis and rate constants from runs at starting pressures of 11 cm. are given in Table 1.

Table 1. *Product distribution (molar) from pyrolysis of methyl nitrite.*

	244°	220°	200°	190°	180°	147°
CH_2O	0·58	0·63	0·68	0·67	0·56	0·52
Me·OH	0·22	0·19	0·21	0·27	0·30	0·46
NO	0·46	0·45	0·69	0·72	0·78	0·96
N_2O	0·22	0·22	0·14	0·12	0·12	0·02
CH_2:N·OH	0·04	0·04	0·01	0	0	0
HCN	0·01	0·02	0	0	0	0
CO	0·09	0·05	0·03	0·03	—	—
N_2	0·04	0·04	—	—	—	—
H_2O	NE	0·32	NE	NE	NE	
10^5k_1 (sec.$^{-1}$) (*a*)	424	68	13·0	5·0	—	—
(*b*)	1190	130	26·7	11·6	—	—

(*a*) Calc. from rate of loss of nitrate. (*b*) Calc. from Steacie and Shaw's data.[1] NE = not estimated.

Rate constants are approximately half those given by Steacie and Shaw;[1] a similar observation has recently been reported by Shaw and Trotman-Dickenson.[6] Analysis carried out at conversions from 7% upwards showed no marked variation in product distribution throughout the reaction at 180—244°. Atom balances were good for nitrogen but usually slightly low for carbon, presumably owing to polymerisation or slight losses of formaldehyde. At 220°, where water was estimated, hydrogen and oxygen balances are also good. A run carried out at 220° with a starting pressure of 3·5 cm. gave results almost identical with those above, and no fall-off in rate was observed.

Results obtained at 220° were very reproducible over long periods in the same reaction vessel, and could readily be repeated in new vessels cleaned in the same way (nitric acid–water). However, after the same vessel had been used for a very long time, a slight decrease in the yield of nitrous oxide was observed at 220° (0·18—0·19 mol.) and a slight brownish film was produced on the vessel walls. Furthermore, in later work with added formaldehyde, it was found that, if the products of reaction were left in the vessel overnight, a brownish-black tar was deposited on the walls. A straight methyl nitrite run carried out in this vessel gave only 0·08 mol. of nitrous oxide with 0·5 mol. of formaldehyde, 0·35 mol. of methanol and 0·8 mol. of nitric oxide, so that it appears that, under special wall conditions, yields of nitrous oxide can be substantially reduced. This was confirmed by subjecting a clean reaction vessel to repeated allyl bromide pyrolysis (cf. Green *et al.*[11]), thereby leaving a heavy carbonaceous layer on the walls, and then using this vessel for normal runs. Analysis of products showed that gross losses of formaldehyde occurred (presumably owing to polymerisation on the walls), but yields of nitrous oxide were substantially reduced whilst the apparent overall reaction rate increased markedly. After one treatment with allyl bromide, the yield of nitrous oxide was 0·03 mol.; with successive treatments this rose and appeared to become constant at about 0·13 mol.

In clean-wall conditions, however, it appears that heterogeneous reactions are unimportant since packing the reaction vessel with Pyrex tubing (S/V increased 8 times) changed neither the overall rate nor the product distribution. In all further work therefore clean-walled reaction vessels were used, and, in studies on the effect of additives on product distribution, the state of the walls was regularly checked by carrying out straight runs on methyl nitrite to confirm that yields of nitrous oxide were normal (*i.e.*, *ca.* 0·22 mol. at 220°).

[11] Green and Maccoll, *J.*, 1955, 2450.

The products obtained at 147° appear to substantiate the results of Steacie and Shaw in that the main reactions can be represented:

$$2MeO{\cdot}NO \longrightarrow CH_2O + MeOH + 2NO$$

but as the temperature is raised, nitrous oxide and, to a smaller extent, formaldehyde increase in amount at the expense of nitric oxide and methanol. Nitrous oxide does not arise from secondary reactions of stable products because it remains virtually constant from about 7% reaction upwards; further, addition of stable reaction products had no effect on this yield.

These observations can be explained on the basis of a mechanism similar to that proposed by Levy [3] for ethyl nitrite, namely:

$$MeO{\cdot}NO \rightleftharpoons MeO{\cdot} + NO{\cdot}$$
$$MeO{\cdot} + NO \longrightarrow CH_2O + HNO$$
$$2HNO \longrightarrow H_2O + N_2O$$
$$2MeO \longrightarrow CH_2O + MeOH$$

in which the nitrous oxide comes from nitroxyl, which itself arises by hydrogen abstraction from methoxyl by nitric oxide. Gray and Williams [5] proposed a similar mechanism of formation of nitrous oxide from methyl nitrite.

The presence of methoxyl radicals in decomposing methyl nitrite can readily be proved by adding a hydrogen-donor. Thus addition of cyclohexene, which as Rust *et al.*[12] have shown is a good donor in the presence of methoxyl radicals (from methyl t-butyl peroxide) at 195°, increases the yields of methanol and nitric oxide and almost eliminates nitrous oxide, at 220° as shown in Table 3 (the rate of loss of nitrite also increases). These changes

TABLE 2. *Effect of added cyclohexene: molar yields.*[a]

MeO·NO : C_6H_{10}	CH_2O	MeOH	NO	N_2O	CO	N_2	10^5k_1 (sec.$^{-1}$)
1 : 1·1	0·34	0·48	0·90	0·03	0·04	0·02	118
1 : 2·8	0·32	0·51	0·96	0·003	0·05	0·02	130

Initial pressure of MeO·NO, 11 cm.

are due to preferential reaction of methoxyl with cyclohexene, and support the view that nitrous oxide is formed by reaction of methoxyl with nitric oxide. The failure of added cyclohexene to eliminate formaldehyde suggests that some of the cyclohexenyl radicals may react with methoxyl to regenerate cyclohexene and formaldehyde. Further evidence was obtained from the effects of added formaldehyde and acetaldehyde. Thus added formaldehyde only very slightly decreased the yield of nitrous oxide at 220°, but yields of methanol and carbon monoxide were markedly greater, as was the rate of loss of nitrite (cf. Table 3). When however acetaldehyde was added, then yields of methanol, nitric oxide, formaldoxime, and hydrogen cyanide were markedly greater but no nitrous oxide was formed; the overall rate of reaction was also markedly greater. These observations are understood on the basis of the reactions:

$$MeO{\cdot} + CH_2O \longrightarrow MeOH + {\cdot}CHO$$
$${\cdot}CHO \longrightarrow H{\cdot} + CO$$
$$H{\cdot} + NO \longrightarrow HNO$$

or

$${\cdot}CHO + NO \longrightarrow HNO + CO$$
$$2HNO \longrightarrow N_2O + H_2O$$

and

$$MeO{\cdot} + Me{\cdot}CHO \longrightarrow MeOH + CH_3{\cdot}CO{\cdot}$$
$$CH_3{\cdot}CO{\cdot} \longrightarrow Me{\cdot} + CO$$
$$Me{\cdot} + NO \longrightarrow MeNO \longrightarrow CH_2{:}N{\cdot}OH \longrightarrow HCN + H_2O$$

[12] Rust, Seubold, and Vaughan, *J. Amer. Chem. Soc.*, 1950, **72**, 338.

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TABLE 3. *Effect of added formaldehyde: molar yields.*[a]

MeO·NO : CH_2O	CH_2O	MeOH	NO	N_2O	CO	10^5k_1 (sec.$^{-1}$)
1 : 0·9	—	0·40	0·51	0·20	0·21	111
1 : 1·9	—	0·62	0·56	0·19	0·30	117

[a] Initial pressure of MeO·NO, 11cm.

Thus for every methoxyl radical which abstracts hydrogen from formaldehyde, one formyl radical is produced which itself reacts with nitric oxide to form nitroxyl, so that, if the rate of the last reaction is comparable with that between methoxyl and nitric oxide, yields of nitrous oxide should be virtually unchanged. On the other hand, there is no plausible way in which acetyl can react with nitric oxide to form nitroxyl; the reaction $Me\cdot CO\cdot + NO \longrightarrow CH_2{:}CO + HNO$ can be excluded because yields of carbon monoxide were greatly increased.

One difficulty with the proposed mechanism of nitrous oxide formation is that Levy [3,13] reported that only very small yields of this oxide were obtained from ethoxyl radicals (formed from diethyl peroxide) and nitric oxide at 180°. Similar results have been obtained by treating dimethyl peroxide with nitric oxide at 180°. Thus in 30 minutes at 180° 35 mm. of dimethyl peroxide decomposed completely to give 1½ mol. of methanol and ½ mol. of carbon monoxide according to the mechanism:

$$Me_2O_2 \longrightarrow 2MeO\cdot$$
$$2MeO\cdot \longrightarrow CH_2O + MeOH$$
$$MeO\cdot + CH_2O \longrightarrow MeOH + \cdot CHO$$
$$MeO\cdot + \cdot CHO \longrightarrow MeOH + CO$$

Since this work was completed similar results have been published by Calvert and Hahnst.[14] A mixture of 35 mm. of peroxide and 145 mm. of nitric oxide after 30 minutes at 180° gave only 0·02 mol. of nitrous oxide per methoxyl formed, the main product being methyl nitrite with smaller proportions of formaldehyde, methanol, and carbon monoxide. Pyrolysis of the nitrite under these conditions is negligible. Nitrogen, however, was not estimated, so the possibility remains that nitroxyl could be formed in large yield and then break down in other ways, *e.g.*, $2HNO \longrightarrow N_2 + 2HO\cdot$. This was disposed of by repeating Levy's work with diethyl peroxide and nitric oxide; nitrogen and nitrous oxide yields were only 0·03 mol. per ethoxyl radical produced.

This apparent anomaly finds ready explanation in the activation energies for the competing reactions in dialkyl peroxide–nitric oxide systems. Thus that forming methyl nitrite, $MeO\cdot + NO \longrightarrow MeO\cdot NO$, should have zero activation energy, but that leading to nitroxyl, $MeO\cdot + NO \longrightarrow HNO + CH_2O$, will certainly be greater than zero. The latter will therefore be favoured by higher temperatures, as is in fact found in pyrolysis of methyl nitrite, and the formation of any nitrous oxide at 180° by reaction between dialkyl peroxides and nitric oxide can be regarded as evidence for the formation of larger yields in this way at higher temperatures. Direct proof cannot be obtained because if peroxide and nitric oxide were allowed to react at, say, 220° pyrolysis of the methyl nitrite formed would yield nitrous oxide.

A further apparent anomaly is that on the basis of the postulated mechanism addition of nitric oxide would be expected to increase the yield of nitrous oxide, whereas no such effect is observed in 1 : 2 nitrite–nitric oxide mixtures, although the yield of formaldehyde increases and that of methanol decreases whilst the rate of loss of nitrite remains virtually unchanged. Again these observations can be explained on the basis of the various reactions competing for methoxyl and will be dealt with below. The above result is in direct contradiction to that of Levy,[3] who found that addition of nitric oxide markedly increased yields of nitrous oxide in the pyrolysis of ethyl nitrite; repetition of Levy's work

[13] Levy, *J. Amer. Chem. Soc.*, 1953, **75**, 1801.
[14] Calvert and Hahnst, *J. Phys. Chem.*, 1959, **63**, 104.

with ethyl nitrite at 200° did not confirm his finding, the yield of nitrous oxide being unchanged by addition of nitric oxide whilst that of acetaldehyde increased and that of ethanol decreased.

The above observations on the effect of nitric oxide refer to the condition where its concentration is relatively large. In the very early stages of pyrolysis without added nitric oxide, it might be expected that yields of nitrous oxide would increase progressively with time because of the build-up of nitric oxide concentration. Some evidence of this has been obtained by studying the reaction at low pressures (2—5 mm.) in a flow system at 295°, as shown in Table 4.

TABLE 4. *Effect of reaction time on yields of nitrous oxide in a flow system.*

Reaction time (sec.)	0·48	0·93	2·0	6·0
Decomposition (%)	3	6	19	45
NO : N_2O	250	220	30	8

An alternative mechanism for formation of nitrous oxide, which may occur conjointly with the nitric oxide–methoxyl reaction, is direct intramolecular elimination of nitroxyl, MeO·NO ⟶ CH_2O + HNO, as postulated for the pyrolysis and photolysis of higher alkyl nitrites.[15] More recently Brown and Pimentel,[16] in matrix isolation studies at 20° K on the photolysis of nitromethane and methyl nitrite, identified nitroxyl by infrared spectroscopy and ascribed it to intramolecular elimination from the *cis*-form of the nitrite, although they do not exclude the possibility of reaction between methoxyl and nitric oxide.

If nitrous oxide is formed by elimination of nitroxyl in this way, it would be expected that the *cis*-form would become more abundant as the temperature was raised because it has been shown above that yields of nitrous oxide increase from 147° to 220°. However, Tarte's infrared data [17] for −80° and +23° suggest that the *trans*-form becomes more abundant as the temperature is raised. This has been confirmed at 25—230°; Table 5 shows the ratios of the optical densities of the 5·95 and 6·15 μ peaks which Tarte has

TABLE 5. *Variation of* cis/trans *ratio, determined from optical densities, with temperature.*

Temp. (c)	−253°	−80°	+25°	+120°	+180°	+230°
cis/trans	1·7 [a]	1·4 [b]	1·13	0·88	0·81	0·71

[a] Ref. 16. [b] Ref. 17.

assigned to the *trans*- and *cis*-$\nu_{N=O}$ vibrations respectively. Intramolecular elimination cannot therefore be supported.

A further possibility for nitroxyl formation involves splitting of the initially formed methoxyl radical:

$$MeO\cdot \longrightarrow CH_2O + H\cdot; \quad \Delta H\ 25\ \text{kcal. mole}^{-1}$$

$$H\cdot + NO \longrightarrow HNO$$

as proposed by Gray and Style [7] in their photolytic work. In their work, however, this reaction was made possible by the excess of energy remaining after irradiation; in the present instance it is unlikely on energetic grounds. Its non-occurrence has been demonstrated by decomposing methyl nitrite in the presence of acetaldehyde, when the reaction H· + Me·CHO ⟶ H_2 + Me·CO· would be expected: no hydrogen was detected in the products.

[15] Purkis and Thompson, *Trans. Faraday Soc.*, 1936, **32**, 1466; Gowenlock, *Chem. Soc. Special Publ., No.* 10, 1957, p. 82.
[16] Brown and Pimentel, *J. Chem. Phys.*, 1958, **29**, 884.
[17] Tarte, *J. Chem. Phys.*, 1952, **20**, 1570.

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Methoxyl radicals not reacting with nitric oxide might react in several ways to give methanol and formaldehyde. The reactions proposed by Steacie and Shaw, namely:

$$MeO\cdot \longrightarrow H\cdot + CH_2O$$
$$H\cdot + MeO\cdot \longrightarrow MeOH$$

can be discounted for reasons given above. Disproportionation has been suggested by several workers, *e.g.*, Powling and Arden,[4] in the sense:

$$2MeO\cdot \longrightarrow CH_2O + MeOH;\ \Delta H\ -75\ \text{kcal. mole}^{-1}$$

and it is energetically very favourable. The abstraction reaction,

$$MeO\cdot + MeO\cdot NO \longrightarrow MeOH + CH_2O + NO;\ \Delta H\ -39\ \text{kcal. mole}^{-1}$$

analogous to that proposed by Phillips [18] for the alkyl nitrates, has been discounted by Levy [13] who showed that ethoxyl did not abstract hydrogen atoms from ethyl nitrite at 180°. This conclusion was based on the fact that no change in ethyl nitrite concentration occurred when mixtures of nitrite and diethyl peroxide were heated for sufficient time completely to decompose the latter. It is, however, not unequivocal because, as Levy showed, nitric oxide produced in the abstraction could react rapidly with the ethoxyl radicals from the peroxide to regenerate ethyl nitrite. In an attempt to resolve this point, diethyl peroxide was heated in the presence of methyl nitrite for sufficient time at 180° to decompose all of the former (under these conditions pyrolysis of the nitrite is negligible). If hydrogen abstraction occurred, then *ethyl* nitrite should be found in the products:

$$EtO\cdot + MeO\cdot NO \longrightarrow EtOH + CH_2O + NO$$
$$NO + EtO\cdot \longrightarrow EtO\cdot NO$$

An initial mixture of 41·4 mm. of methyl nitrite and 21·1 mm. of diethyl peroxide gave 38·0 mm. of methyl nitrite and 2·7 mm. of ethyl nitrite. Control experiments showed that no ethyl nitrite was formed by exchange between ethanol (from the peroxide) and methyl nitrite. It appears, therefore, that only about 6·5% of the ethoxyl radicals produced abstract hydrogen from methyl nitrite. Since even this evidence might be confused by exchange between ethoxyl and the methyl nitrite, ethoxyl (from the peroxide) was allowed to react with $[^2H_3]$methyl nitrite. $[^2H_1]$Ethanol, estimated mass spectrometrically, amounted to about 8% of the available ethoxyl radicals; this is in good agreement with the above result. Therefore, on the assumption that the reactivities of methoxyl and ethoxyl are similar, it is considered that hydrogen abstraction from methyl nitrite at 180° is very slow.

Another reaction possibly leading to methanol is that proposed by Levy: [3]

$$MeO\cdot + HNO \longrightarrow MeOH + NO;\ \Delta H\ -14\ \text{kcal. mole}^{-1}$$

This appears feasible, especially as Dalby [19] has shown that nitroxyl has a comparatively long life, but, on balance, it is considered that the energetically more favourable disproportionation of methoxyl is more likely.

Whilst, therefore, it appears that, in the temperature range studied, methoxyl radicals preferentially disproportionate rather than abstract hydrogen from the nitrite, at higher temperatures the position may be reversed since Wijnen [20] has shown that hydrogen abstraction from methyl acetate by methoxyl requires an activation energy of 4·5 kcal. mole^{-1}, to be compared with the expected zero for disproportionation.

[18] Phillips, *Nature*, 1947, **160**, 753; Ph.D. Thesis, London, 1949.
[19] Dalby, *Canadian J. Phys.*, 1958, **10**, 1336.
[20] Wijnen, *J. Chem. Phys.*, 1948, **16**, 353.

The origin of the small amounts of formaldoxime produced at 220° is obscure, but a possibility is:

$$MeOH + HNO \longrightarrow Me{\cdot}NO + H_2O$$
$$Me{\cdot}NO \longrightarrow CH_2{:}N{\cdot}OH$$

Gowenlock and Lüttke [21] have pointed out that *C*-nitroso-compounds can react in this way; nitroxyl might react similarly. Some evidence for this is found in the fact that added cyclohexene, which eliminates formation of nitrous oxide, also eliminates that of formaldoxime. The small amounts of carbon monoxide formed clearly come from methoxyl attack on formaldehyde, since they are greatly increased by addition of the latter. Ethylene glycol, stated [22] to be formed by methoxyl attack on methanol at 160°, was not detected.

The reaction mechanism for pyrolysis of methyl nitrite at 180—240° can therefore be represented as follows:

$$MeO{\cdot}NO \longrightarrow MeO{\cdot} + NO \quad . . . . . (1)$$
$$MeO{\cdot} + NO \longrightarrow MeO{\cdot}NO \quad . . . . . (2)$$
$$MeO{\cdot} + NO \longrightarrow CH_2O + HNO \quad . . . . . (3)$$
$$2MeO{\cdot} \longrightarrow MeOH + CH_2O \quad . . . . . (4)$$
$$2HNO \longrightarrow (HNO)_2 \quad . . . . . (5)$$
$$(HNO)_2 \longrightarrow N_2O + H_2O \quad . . . . . (6)$$
$$MeO{\cdot} + MeO{\cdot}NO \longrightarrow MeOH + CH_2O + NO \quad . . . . . (7)$$
$$MeO{\cdot} + CH_2O \longrightarrow MeOH + {\cdot}CHO \quad . . . . . (8)$$
$$MeO{\cdot} + {\cdot}CHO \longrightarrow MeOH + CO \quad . . . . . (9)$$

(Reactions leading to small amounts of nitrogen and formaldoxime have been ignored for simplicity of kinetic treatment. The decomposition of nitroxyl into nitrous oxide and water is written as an association followed by a first-order process.[23])

Kinetic analysis of this scheme has to account for the following facts observed at 220°: (*a*) the rate of disappearance of nitrite is of first-order and is substantially unaffected by addition of nitric oxide, (*b*) the rate of formation of nitrous oxide is independent of nitric oxide concentration (except possibly in the early stages of reaction), (*c*) methanol formation is suppressed by addition of nitric oxide, (*d*) formaldehyde yields are, at the most, only slightly increased by addition of nitric oxide, and (*e*) the rate of disappearance of nitrite is increased by addition of hydrogen-donors.

A stationary-state treatment leads to a quadratic expression for methoxyl concentration which would be too cumbersome for simple use. The partial solution

$$[MeO{\cdot}] = \frac{k_1[MeO{\cdot}NO]}{(k_2 + k_3)\,[NO] + k_4[MeO{\cdot}] + 2k_8[CH_2O] + k_7[MeO{\cdot}NO]}$$

is however sufficient, and leads to:

$$-R_{MeO{\cdot}NO} = k_1[MeO{\cdot}NO] + \frac{k_1k_7[MeO{\cdot}NO]^2 - k_1k_2[MeO{\cdot}NO][NO]}{(k_2 + k_3)[NO] + k_4[MeO{\cdot}] + 2k_8[CH_2O] + k_7[MeO{\cdot}NO]}$$

Since reaction (7) is relatively slow, and carbon monoxide yields are relatively small (except when formaldehyde is added),

$$(k_2 + k_3)[NO] + k_4[MeO{\cdot}] \gg 2k_8[CH_2O] + k_7[MeO{\cdot}NO];$$

hence $$-R_{MeO{\cdot}NO} \approx k_1[MeO{\cdot}NO] + \frac{k_1k_7[MeO{\cdot}NO]^2 - k_1k_2[MeO{\cdot}NO][NO]}{[NO]\{(k_2 + k_3) + k_4[MeO{\cdot}]/[NO]\}}$$

[21] Gowenlock and Lüttke, *Quart. Rev.*, 1958, **12**, 321.
[22] Takezaki and Takeuchi, *J. Chem. Phys.*, 1954, **22**, 1527.
[23] Cf. Harteck, *Ber.*, 1933, **66**, 423.

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Now [NO] will be much larger than [MeO·] except in the early stages of reaction, so

$$-R_{\mathrm{MeO\cdot NO}} \approx k_1k_3[\mathrm{MeO\cdot NO}]/(k_2 + k_3),$$

which satisfies point (*a*).

Similarly, the rate of formation of nitrous oxide can be shown to be:

$$R_{\mathrm{N_2O}} \approx \frac{\frac{1}{2}k_1k_3[\mathrm{MeO\cdot NO}]}{(k_2 + k_3) + k_4[\mathrm{MeO\cdot}]/[\mathrm{NO}]}$$

which, except in the very early stages of reaction, reduces to:

$$R_{\mathrm{N_2O}} \approx k_1k_3[\mathrm{MeO\cdot NO}]/2(k_2 + k_3),$$

which satisfies point (*b*). In the very early stages of reaction, $k_4[\mathrm{MeO\cdot}]/[\mathrm{NO}]$ would become appreciable with respect to $(k_2 + k_3)$, and nitrous oxide formation would then show dependence on nitric oxide concentration. This might explain the results obtained under flow conditions.

In a similar manner it can be shown that methanol formation is inversely proportional to, and that of formaldehyde is substantially independent of, nitric oxide concentration. In the presence of an added hydrogen, the reaction

$$\mathrm{MeO\cdot} + \mathrm{RH} \longrightarrow \mathrm{MeOH} + \mathrm{R} \quad \ldots\ldots\ldots\ldots \quad (10$$

must be introduced; the rate of loss of nitrite becomes

$$-R_{\mathrm{MeO\cdot NO}} = k_1[\mathrm{MeO\cdot NO}] - \frac{k_1k_2[\mathrm{MeO\cdot NO}][\mathrm{NO}]}{(k_2 + k_3)[\mathrm{NO}] + k_4[\mathrm{MeO\cdot}] + k_{10}[\mathrm{RH}]}$$

With good donors (*e.g.*, cyclohexene, aldehydes), $k_{10}[\mathrm{RH}]$ becomes relatively very large, so that the above expression tends to

$$-R_{\mathrm{MeO\cdot NO}} = k_1[\mathrm{MeO\cdot NO}],$$

i.e., the rate of loss of nitrite increases.

The reaction mechanism given above thus accounts for all the major experimental findings.

The temperature-dependence of the rate of loss of nitrite gives the relation:

$$k = 10^{12\cdot2} \exp(-34{,}300/\boldsymbol{R}T) \text{ (sec.}^{-1}\text{)}$$

as compared with

$$k = 1\cdot84 \times 10^{13} \exp(-36{,}400/\boldsymbol{R}T) \text{ (sec.}^{-1}\text{)}$$

found by Steacie and Shaw.[1] Activation energies for the pyrolysis of alkyl nitrites are usually equated with the O–N bond energy.[24] The kinetic analysis developed herein shows that the first-order rate constant approximates to $k_1k_3/(k_2 + k_3)$ which can only equal k_1 if $k_2 \ll k_3$ which is certainly not true since the rate of recombination of methoxyl and nitric oxide is high. The apparent activation energy can at the best be only a rough approximation of the O–N bond energy.

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Explosives Research and Development Establishment, Ministry of Aviation,
Waltham Abbey, Essex. [*Received, October 17th*, 1960.]

[24] Gray and Williams, *Chem. Rev.*, 1959, **59**, 250.

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592. *The Infrared Spectra of Some Transition-metal Perchlorates.*

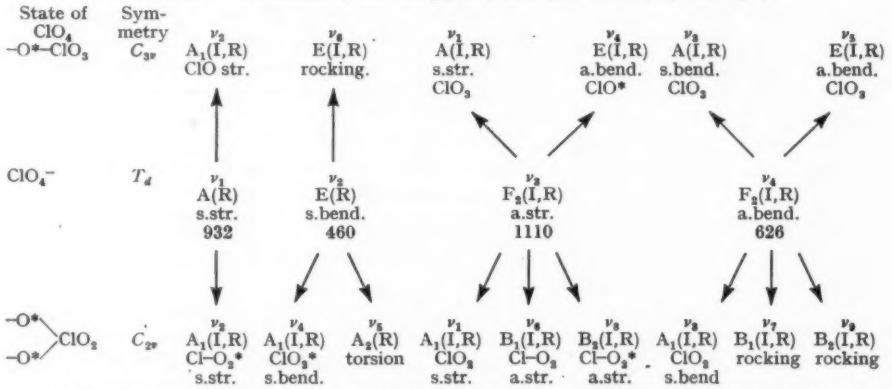
By B. J. Hathaway and A. E. Underhill.

The infrared spectra of some hydrated transition-metal perchlorates, some transition-metal perchlorate–methyl cyanide complexes, and anhydrous copper perchlorate are reported. The spectra are interpreted in terms of ionic perchlorate and perchlorato-groups.

As a result of the observation that anhydrous cupric perchlorate is volatile [1] the infrared spectrum of this and some transition-metal perchlorate complexes have been examined to obtain evidence of the formation of the metal–perchlorate bond in the solid state.

The infrared spectra of a number of ionic perchlorates are listed by Miller and Wilkins.[2] The Raman spectrum of the perchlorate ion has been studied by several investigators,[3,4] and apart from minor differences in the numerical values accepted for its fundamentals their assignments have been established. The perchlorate ion has a regular tetrahedral structure and belongs to the point group T_d, having nine vibrational degrees of freedom distributed between four normal modes of vibration. The assignments of these modes are listed in Table 1. In general the triply degenerate frequencies ν_3 and ν_4 are observed

Table 1. *Vibrations of the* ClO_4 *group as a function of symmetry.*†



† A and B, non-degenerate. E, doubly degenerate. F, triply degenerate. I, infrared active. R, Raman active. s., symmetric. a., antisymmetric. O* refers to oxygen co-ordinated to copper.

in the infrared spectra of ionic perchlorates, the former appearing as a very broad strong band with a poorly defined maximum, which is occasionally split.[2] The non-degenerate frequency ν_1, which is theoretically forbidden in the infrared, usually occurs as a very weak absorption at 930 cm.$^{-1}$. This absorption becomes weakly allowed owing to distortion of the ion in a crystal field of lower symmetry than itself.

If the perchlorate group changes from an ionic to a perchlorato-group, *i.e.*, is involved in partial covalent bonding between one of its oxygen atoms and a cation, this oxygen atom is no longer equivalent to the other three and the original T_d symmetry of the perchlorate ion is lowered to C_{3v}. Table 1 illustrates the correlation between the vibrations of a molecule with T_d symmetry and those of its derivative of C_{3v} symmetry. The numerical values of the fundamental frequencies in a perchlorato-group with C_{3v} symmetry

[1] Hathaway, *Proc. Chem. Soc.*, 1958, 344.
[2] Miller and Wilkins, *Analyt. Chem.*, 1952, **24**, 1253.
[3] Landolt–Börnstein, "Zahlenwerte und Funktion," Springer-Verlag, Berlin, 1951, I Band, 2 Teil, Molekeln I, pp. 152, 259.
[4] Cohn, *J.*, 1952, 4282.

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cannot be predicted with accuracy. However, the values for anhydrous perchloric acid [5] and perchloryl fluoride,[6] both of which have C_{3v} symmetry, can be taken as a useful guide. These values are given as follows:

	ν_1	ν_2	ν_3	ν_4	ν_5	ν_6
$HClO_4$	1032	739	574	1312	585	426
ClO_3F	1061	715	549	1315	589	405
$O{\cdot}SO_3^{2-}$	1038	970	645	1130	604	438

The shift from 932 cm.$^{-1}$ (ν_1) of the ionic perchlorate to 739 and 715 cm.$^{-1}$ (ν_2) of perchloric acid and perchloryl fluoride, respectively, is rather large but is consistent with the radical differences between the symmetrical ClO stretching vibration of the ionic perchlorate and that of the ClF and ClOH bonds. Such a radical shift in this frequency would not be expected in the perchlorato-group, as the oxygen atom involved in co-ordination is similar to the remaining three oxygen atoms because it is not involved in a complete covalent bond to a cation. Evidence to support this is found in the case of the sulphate ion,[7] the corresponding shift being 981 (T_d) to 970 cm.$^{-1}$ (C_{3v}).

If the perchlorate group occupies a position in a crystal lattice where two of its oxygen atoms are involved in partial covalent bond formation to a cation, or, more probably, to two separate cations, the symmetry of the perchlorate group is lowered to C_{2v}. Table 1 illustrates the correlation between the vibrations of a molecule with T_d symmetry and its C_{2v} derivative. These correlations have been determined by analogy with the sulphate ion when this group is acting as a monodentate (C_{3v}) and bidentate (C_{2v}) ligand.[7] The modes of vibration were assigned by comparison with the assignment for sulphuryl difluoride,[8] and a guide to their numerical values was obtained by comparison with the known values of a bidentate sulphate ion [7] and sulphuryl difluoride,[8] as follows:

	ν_1	ν_2	ν_3	ν_4	ν_5	ν_6	ν_7	ν_8	ν_9
SO_4^{2-}	1055	995	641	462	*	1105	610	1170	571
SO_2F_2	1269	848	544	~300	*	1502	553	885	539

* Raman active only.

The analogy between the bidentate sulphate group and the bidentate perchlorate group should be very close, and the figures for the sulphate should be a much better guide than those of the sulphuryl difluoride.

While the effect of co-ordination of the perchlorate group is likely to bring about major differences in the infrared spectra, minor shifts or splittings may result from a lowering of the site symmetry of the group, from coupling of vibrations between perchlorate groups in the same unit cell, or by a purely isotopic effect within the group.

Results and Discussion

Normal Hydrated Transition-metal Perchlorates.—In Table 2 are recorded the infrared spectra of some hydrated transition-metal perchlorates. They consist of a strong broad

Table 2. *Some hydrated transition-metal perchlorates.*

$Fe(ClO_4)_2,9H_2O$	2040wb			1200—1030s, b	935
$Ni(ClO_4)_2,6H_2O$				1190—1030s, b	930w
$Cu(ClO_4)_2,6H_2O$	2020w			1160—1085s, b	947w, sh 800vw
$Ag(ClO_4),H_2O$	2037s	1985s	1320m	1160—1030s, b	930w
$Th(ClO_4)_4,6H_2O$	2030w		1310m	1160—1105s, b	940w, sh 800vw

v = very. s = strong. b = broad. m = medium. w = weak. sh = shoulder. sp = sharp.

absorption at 1200—1030 cm.$^{-1}$ (ν_3), a very weak absorption at 950—930 cm.$^{-1}$ (ν_1), and a rising absorption at 650 cm.$^{-1}$ due to a peak at about 620 cm.$^{-1}$ (ν_4) which lies outside

[5] Ref. 3, pp. 551, 153.
[6] Lide and Mann, *J. Chem. Phys.*, 1956, **25**, 1128; Powell and Lippincott, *J. Chem. Phys.*, 1960, **32**, 1883.
[7] Nakamoto, Fujita, Tanaka, and Kobayashi, *J. Amer. Chem. Soc.*, 1957, **79**, 4904.
[8] Perkins and Kent Wilson, *J. Phys. Chem.*, 1952, **20**, 1792.

the region studied. The spectra are consistent with a simple perchlorate ion in these salts.

Transition-metal Perchlorate–Methyl Cyanide Complexes.—In Table 3 are recorded the infrared spectra of some transition-metal perchlorate–methyl cyanide complexes. A broad strong absorption still occurs in the region 1200—1000 cm.$^{-1}$ but its width increases in the sequence cobalt, copper, manganese, and zinc. In the last case it is just resolved

TABLE 3. *Transition-metal perchlorate–methyl cyanide complexes.*

$Cu(ClO_4)_2$,4MeCN	$Co(ClO_4)_2$,6MeCN	$Mn(ClO_4)_2$,4MeCN	$Zn(ClO_4)_2$,4MeCN
2325s	2310s	2300s	2320s
2315s	2285s	2285s	2290s
2040w	2030vw		2060vw
	1725		1728w
	1641w	1628w	1628w
1370m	1370m	1370m	1370m
1312vw	1312vw	1315vw	1305vw
	1285vw		
			1200sh
	1143s	1148vs	1150vs
1125vs	1103vs	1130sh	
1065w, sh	1050sh	1060vs	
1038vs		1038sh	1028vs
958w, sp	948w	940m, sp	954w
937w, sp	937vw		948w
			927s, sp
800w	800w	800w	800w
	740w	787w	
671vw	675vw	675vw	658m

into two broad strong peaks at 1150 and 1029 cm.$^{-1}$. The absorption at 950—925 cm.$^{-1}$ increases in intensity and in its degree of splitting in the same sequence. This suggests that the perchlorate group in these complexes may be present not as an ionic species, but as a weakly co-ordinated group, the extent of co-ordination increasing in the above sequence until at zinc the ionic ν_3 band is just resolved into the ν_4 and ν_1 vibrations of the monodentate perchlorate group. The cobalt complex is the least covalent of these four complexes as it contains six methyl cyanide molecules per cobalt ion, in contrast to four in the other complexes. These are probably arranged octahedrally around the cobalt ion and prevent co-ordination by the perchlorate group. In the zinc, copper, and manganese complexes the four methyl cyanide molecules are almost certainly arranged in a square-coplanar configuration around the metal ion, with the perchlorate groups above and below this plane. In the copper complex the otherwise regular octahedral arrangement will be distorted by the Jahn–Teller effect [9] to give a slightly longer bond between the perchlorate groups and the copper ion. This will result in less covalent character in the copper–oxygen bond, and the perchlorate group will be more ionic than in the zinc and manganese complexes. In the zinc and manganese complexes a regular octahedral configuration is likely as they have a d^{10} and d^5 electron configuration, respectively, neither of which is distorted by the Jahn–Teller effect. It is not understood why the zinc compound should contain a perchlorate group with more covalent character than the manganese compound. In the zinc complex the T_d symmetry of the perchlorate group is lowered slightly towards a C_{3v} symmetry, indicating that the bonding between the oxygen of the perchlorate group and the zinc ion is only weak.

The split absorption at 2300 cm.$^{-1}$ in the methyl cyanide complexes is due to the $-C\equiv N$ vibration, which is shifted to slightly higher frequencies than the normal absorption at 2248 cm.$^{-1}$ in methyl cyanide. A similar shift has been observed for co-ordinated methyl cyanide.[10]

Transition-metal Perchlorates: Lower Hydrates.—In Table 4 are listed the main infrared

[9] Orgel and Dunitz, *Nature*, 1957, **179**, 462.
[10] Coerver and Curran, *J. Amer. Chem. Soc.*, 1958, **80**, 3522.

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absorption frequencies in the sodium chloride region of the lower hydrates of iron, nickel, and copper perchlorate, and of copper perchlorate dihydrate in the potassium bromide region. The spectra are completely different from those of the normal hydrates shown in Table 2. They all contain two very strong, well-resolved, peaks between 1200 and 1000 cm.$^{-1}$ and an equally strong peak between 940 and 890 cm.$^{-1}$. From these spectra

TABLE 4. *Transition-metal perchlorates: lower hydrates.*

Sodium chloride region								
$Fe(ClO_4)_2,4H_2O$	2010w			1310w, sh	1160s	1025s	898—865mb	672w
$Ni(ClO_4)_2,2H_2O$	2025w	1915w		1298w, sh	1135s	1035s	937m	660sh
$Cu(ClO_4)_2,2H_2O$	2057w	1930w	1820w		1158vs	1030vs	920vs	660w
Potassium bromide region								
$Cu(ClO_4)_2,2H_2O$		648s	620s	605s		480m	460w	

it seems that the T_d symmetry of the ionic perchlorate present in the normal hydrate has been lowered almost completely to that of C_{3v}, and that the perchlorate groups are co-ordinated through a single oxygen atom to the transition-metal ion. The strong absorption, for example, of copper perchlorate dihydrate at 920 cm.$^{-1}$ can be assigned to the non-degenerate Cl–O* symmetrical stretching frequency ν_2, that at 1158 cm.$^{-1}$ as the doubly degenerate ClO* antisymmetrical bending frequency ν_4, and that at 1030 cm.$^{-1}$ as the non-degenerate ClO_3 symmetrical stretching frequency ν_1 of the monodentate perchlorate group. To obtain confirmation of this interpretation, copper perchlorate dihydrate was also examined in the potassium bromide region, and showed three strong bands, at 648, 620, and 605 cm.$^{-1}$, a medium band at 480 cm.$^{-1}$, and a weak band at 460 cm.$^{-1}$. The absorption at 648 cm.$^{-1}$ can be assigned to the non-degenerate ClO_3 symmetrical bending frequency ν_3, those at 620 and 605 cm.$^{-1}$ to the doubly degenerate ClO_3 antisymmetrical bending frequency ν_5 which is split, and that at 480 cm.$^{-1}$ to the doubly degenerate rocking frequency ν_6, of the monodentate perchlorato-group. It is uncertain why the ν_5 vibration should be split, but a similar effect was obtained with anhydrous copper perchlorate and is discussed below. The three strong bands in the potassium bromide region, in contrast to the single absorption of an ionic perchlorate, support the interpretation of the bands in the sodium chloride region as due to a covalently bonded perchlorate group with C_{3v} symmetry.

The change in the spectra of the dihydrates compared with hexahydrates is too large to be interpreted as a change of site symmetry of the perchlorate group in the crystal lattice. As water is removed from the crystal lattice of the hexahydrate the holes left must allow the perchlorate groups to move so that they can co-ordinate to the metal ions. If the perchlorate groups are monodentate in the dihydrate lattice the copper ions are four-co-ordinated by two oxygen atoms from water molecules and two from perchlorate groups. This type of four co-ordination for copper is unusual, as cupric copper is usually octahedral with four equivalent short bonds and two slightly longer bonds.[9] However, in the dihydrate crystal factors may not allow the perchlorate groups to rearrange and act as bidentate ligands to give the preferred distorted octahedron.

Copper perchlorate dihydrate, prepared by the action of anhydrous perchloric acid on anhydrous copper nitrate,[11] has the same spectra as that prepared by dehydration.

Anhydrous Transition-metal Perchlorates.—In Table 5 are listed the main infrared absorption frequencies of sublimed copper perchlorate and anhydrous ferric perchlorate. The spectrum of copper perchlorate in the sodium chloride region has three strong absorptions, at 1270—1245, 1130, and 948—920 cm.$^{-1}$, and a weak one at 1030 cm.$^{-1}$. This spectrum differs radically from that of the normal hydrated perchlorate (Table 2) and significantly from those of the lower hydrates. For comparison the three types of spectra

[11] Hathaway and Underhill, *J.*, 1960, 648.

for the copper salts are shown in the Figure. It seems that the symmetry of the perchlorate groups has been lowered to C_{2v} and indicates that they are acting as bidentate ligands through two of their oxygen atoms. The completeness of this transition suggests

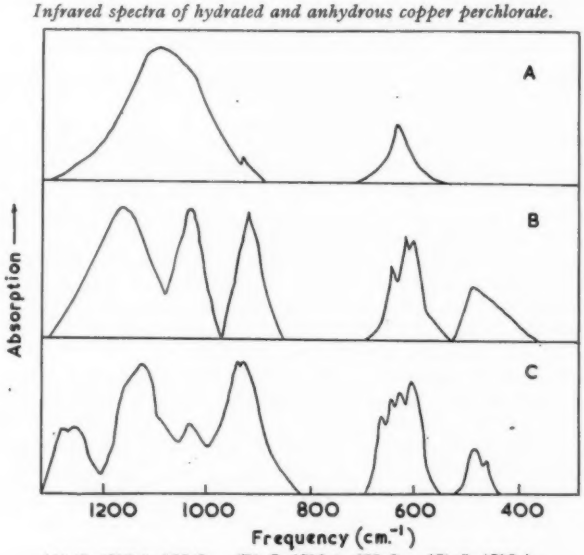
TABLE 5. *Anhydrous transition-metal perchlorates.*

	$Cu(ClO_4)_2$	$Fe(ClO_4)_{2\cdot6}(NO_2)_{0\cdot4},0\cdot2NO_2ClO_4$*		$Cu(ClO_4)_2$	$Fe(ClO_4)_{2\cdot6}(NO_2)_{0\cdot4},0\cdot2N_2ClO_4$*
	1350vw	1605vw	ν_3	665m	662m
ν_8	1270—1245sb	1285sb		647m	—
ν_6	1130s	1160s	ν_7	624m	—
ν_1	1030w	1018w		600s	—
ν_2	948s	922s	ν_9	497m	—
	920s	893sh	ν_4	466w	—

* See Experimental section, p. 3096.

that the perchlorate groups are quite strongly co-ordinated to the transition-metal ion. For anhydrous copper perchlorate with C_{2v} symmetry, the absorption at 948—920 cm.$^{-1}$ is assigned to the non-degenerate ClO_2* symmetrical stretching frequency ν_2, that at 1270—1245 cm.$^{-1}$ to the non-degenerate ClO_2* antisymmetric stretching frequency ν_8, that at

Infrared spectra of hydrated and anhydrous copper perchlorate.



(A) $Cu(ClO_4)_2,6H_2O$. (B) $Cu(ClO_4)_2,2H_2O$. (C) $Cu(ClO_4)_2$.

1130 cm.$^{-1}$ to the non-degenerate ClO_2 antisymmetric stretching frequency ν_6, and that at 1030 cm.$^{-1}$ to the non-degenerate ClO_2 symmetrical stretching frequency ν_1. Similar assignments can be made for ferric perchlorate in this region. It is not known why the vibration ν_1 should be so weak compared with the corresponding one of the monodentate perchlorate group. The infrared absorption frequencies in the potassium bromide region of anhydrous copper perchlorate are shown in Table 5 and consist of one strong, four medium, and one weak band. For a bidentate perchlorate group four bands would be expected theoretically in this region, but as there are six some must involve splitting. The two bands at 665 and 647 cm.$^{-1}$ are tentatively assigned to the non-degenerate ClO_2 symmetrical bending frequency ν_3, those at 624 and 600 cm.$^{-1}$ to the non-degenerate rocking frequency ν_7, and that at 497 cm.$^{-1}$ to the non-degenerate rocking frequency ν_9. The weak absorption at 466 cm.$^{-1}$ is assigned to the non-degenerate ClO_2* symmetrical bending

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frequency ν_4. The assignment of these vibrations has been made mainly by comparison with the corresponding vibration of the bidentate sulphate ion [7] and sulphuryl difluoride.[8]

The splitting which occurs with anhydrous copper perchlorate and to a smaller extent for the dihydrate may be due to the presence of the ^{35}Cl and ^{37}Cl isotopes of chlorine although in this case it would be expected to be less than 10 cm.$^{-1}$. Alternatively, it may be due to coupling of vibrations between two separate perchlorate ions. A similar coupling occurs with uranyl nitrate hydrate.[12]

Experimental

Determination of Spectra.—A Unicam S.P. 100 infrared spectrophotometer was used for measurements in the sodium chloride region, and a Perkin–Elmer 21 instrument for those in the potassium bromide region. All spectra were for mulls in Nujol (5000—400 cm.$^{-1}$) or hexachlorobutadiene (regions obscured by Nujol).

The mull plates were protected from the mull by thin films of polythene,[13] which was necessary for work with perchlorates as these compounds react with the windows to give the spectrum of the perchlorate ion.

The mull samples were prepared and placed between the potassium bromide plates, and the plates mounted in the plate holder, in a dry box.

Preparation of Compounds.—The normal hydrated transition-metal perchlorates were obtained by standard procedures. The lower hydrates were obtained by heating the normal hydrates under a vacuum to constant weight, at ~100°, with care to avoid decomposition to the basic salt.

Anhydrous copper perchlorate was prepared [1] by the repeated reaction under a vacuum of nitrosyl perchlorate on copper perchlorate dihydrate, followed by fractional vacuum-sublimation of the product at 200° under a vacuum between each reaction. The hygroscopic pale green crystals of anhydrous copper perchlorate were separated from the emerald-green crystals of copper nitrate perchlorate, by hand in a dry box [Found: Cu, 24·1; ClO_4, 75·7. Calc. for $Cu(ClO_4)_2$: Cu, 24·1; ClO_4, 75·9%]. Impure ferric perchlorate was obtained by reaction of nitrosyl perchlorate on anhydrous ferric chloride at 200°: it could not be purified by fractional sublimation but was heated at 180° under a vacuum to decompose the excess of nitronium perchlorate. The residue was a red-brown solid which contained 85% of ferric perchlorate. Analysis gave the formula $Fe(ClO_4)_{2\cdot6}(NO_2)_{0\cdot4},0\cdot2NO_2ClO_4$.

The methyl cyanide complexes of copper,[14] cobalt, manganese, and zinc perchlorate were obtained by treating a suspension of nitrosyl perchlorate in methyl cyanide with the respective metal under reduced pressure for 4—6 hr. The resulting solution of the metal perchlorate in methyl cyanide was then evaporated to dryness under a vacuum to yield the metal perchlorate–methyl cyanide *complexes* [Found: Co, 11·3; ClO_4, 38·0. $Co(ClO_4)_2,C_{12}H_{18}N_6$ requires Co, 11·7; ClO_4, 39·5. Found: Zn, 15·0; ClO_4, 45·5. $Zn(ClO_4)_2,C_8H_{12}N_4$ requires Zn, 15·38; ClO_4, 46·4. Found: Mn, 13·2; ClO_4, 46·7. $Mn(ClO_4)_2,C_8H_{12}N_4$ requires Mn, 13·1; ClO_4, 47·6%].

The authors are indebted to Dr. G. W. Gray for the infrared measurements in the sodium chloride region, to Dr. D. Sharp (Imperial College, London) and Dr. H. Fritz (University, München) for measurements in the potassium bromide region, to the Chemical Society for a grant for apparatus, and to the Department of Scientific and Industrial Research for a maintenance grant (to A. E. U.).

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[12] Gatehouse and Comyns, *J.*, 1958, 3965.
[13] Vratny, *Appl. Spectroscopy*, 1959, **13**, 59.
[14] Hathaway and Underhill, *J.*, 1960, 3705.

593. *Kinetics and Mechanism of Oxidation of Mandelic, DL-Malic, and Lactic Acid by Ceric Sulphate.*

By B. Krishna and K. C. Tewari.

The mechanism proposed by Waters for the oxidation of α-hydroxy-acids by manganic pyrophosphate accounts for the kinetics of oxidation of mandelic, DL-malic, and lactic acid by ceric sulphate. The reactants pass through a cyclic transition state involving the hydroxy-acid and cerium(IV). It is suggested that the reactive species of cerium is $Ce(SO_4)_2$ and that the HSO_4^- ion plays the rôle of an active inhibitor by forming $H_2Ce(SO_4)_4^{2-}$ on reacting with the sulphate.

The kinetics and mechanism of oxidation of organic acids by ceric sulphate have not been adequately studied, though Benrath and Ruland [1] showed that oxidation of tartaric, malonic, citric, and oxalic acid by ceric sulphate is not of simple kinetic order. We have studied the oxidation of mandelic, DL-malic, and lactic acid by ceric sulphate in presence of varying amounts of sulphuric acid. Existing data on cerium(IV) complexes occurring in this medium permit elucidation of the mechanism of these oxidations.

Experimental

The materials employed were of the highest purity available (" AnalaR " or E. Merck's Guaranteed Reagent).

A solution [2] of ceric sulphate in 1 : 1 v/v sulphuric acid was diluted and standardized by titration against ferrous ammonium sulphate, *N*-phenylanthranilic acid being used as indicator. The solutions of organic acids were standardized by titration against sodium hydroxide. The progress of the reaction was followed as for the reaction between ceric ion and thallous ion.[3]

To determine the amount of ceric ion consumed, reaction mixtures in which the molar concentration of cerium was 10—15 times that of the acid were left in a thermostat-bath at 25° for several days,[4] after which the amount of ceric salt was determined by titration against ferrous ammonium sulphate. The average of five determinations in each case showed that 1 mole of mandelic, DL-malic, and lactic acid requires 2·0, 8·50, and 5·75 equivalents, respectively, of ceric ion. These values were used in calculating the normality of the acid used in the reaction mixture.

Order of the Reaction.—The reaction is of simple kinetic order if the molar concentration of ceric sulphate is not greater than that of the hydroxy-acid. A plot of log $[(a - x)/(b - x)]$ against time is a straight line (Fig. 1), which implies that the total order of the reaction is two. Here a and b are the initial concentrations of the reactants in terms of the titres of ceric sulphate required by 10 ml. of the reaction mixture. The second-order constant k_2 obtained from the graph represents the specific rate constant in terms of titre values of ceric sulphate and thus depends on the strength (S) of the titrating solution and the volume (V) of the reaction mixture titrated. To compare one experiment with another the value of k_2 is converted into a standard form k_s by multiplying k_2 by V/S. Some results are presented in Table 1. They show that k_s

Table 1. " *Standard* " k_s (*in* l. g.-equiv.$^{-1}$ min.$^{-1}$) *for oxidation of organic acids.*

Lactic acid $[H_2SO_4]$ 0·6N; 25°			Mandelic acid $[H_2SO_4]$ 2·0N; 20°			Malic acid $[H_2SO_4]$ 0·75N; 25°		
$[Ce(SO_4)_2]$ (10^{-3}N)	[Lactic] (10^{-3}N)	10^3k_s	$[Ce(SO_4)_2]$ (10^{-3}N)	[Mandelic] (10^{-3}N)	10^3k_s	$[Ce(SO_4)_2]$ (10^{-3}N)	[Malic] (10^{-3}N)	10^3k_s
1	28·75	34·4	1	1	339	1	10·625	134
1	57·75	34·1	1	2	346	1	21·250	132·5
1	115	34·8	2	1	318	1	42·50	121·5
0·5	57·5	39·6	0·5	1	359	0·5	21·250	151
2	57·5	33·45						

[1] Benrath and Ruland, *Z. anorg. Chem.*, 1920, **114**, 267.
[2] Krishna and Sinha, *Z. phys. Chem.* (*Frankfurt*), 1959, **212**, 149.
[3] Krishna and Sinha, *Z. phys. Chem.* (*Frankfurt*), 1959, **212**, 155.
[4] Shorter and Hinshelwood, *J.*, 1950, 3277.

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is sensibly constant in each case, and that the total order of the reaction is two (unity with respect to each reactant).

Inhibitory Action of Sulphuric Acid and Sulphates.—An important feature of the reaction is that the rate is inversely proportional to the square of concentration of sulphuric acid present

FIG. 1.

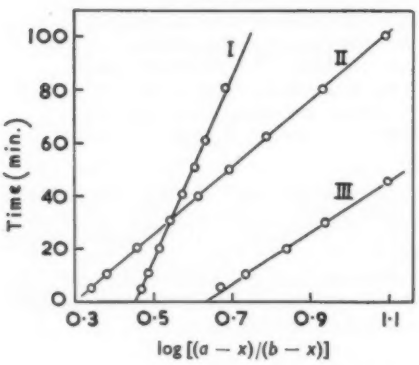


FIG. 2.

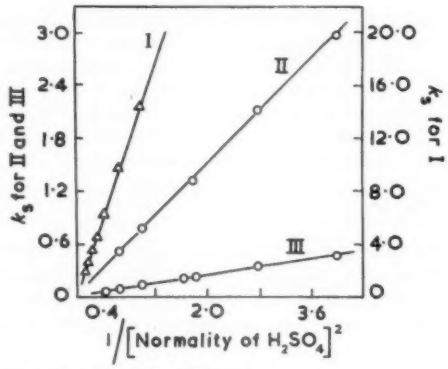


FIG. 1. *Reactions of hydroxy-acids with ceric sulphate.*

	Lactic (I)	Mandelic (II)	Malic (III)
$[Ce(SO_4)_2]$ (10^{-2}N)	10	5	5
[Acid] (10^{-2}N)	2·875	1	2·125
$[H_2SO_4]$ (N)	0·6	2·0	0·75
Temp.	25°	20°	25°

FIG. 2. *Dependence on sulphuric acid concentration.*

	Mandelic (I)	Malic (II)	Lactic (III)
$[Ce(SO_4)_2]$ (10^{-2}N)	1	1	1
[Acid] (10^{-2}N)	1	2·125	5·75
Temp.	20°	25°	25°

TABLE 2. *Dependence of "standard" k_s (in* l. g.-equiv.$^{-1}$ min.$^{-1}$*) on sulphuric acid concentration in oxidation of organic acids.*

Lactic acid: $5·75 \times 10^{-2}$N; $Ce(SO_4)_2$: 10^{-2}N; 25°		Mandelic acid: 10^{-2}N; $Ce(SO_4)_2$: 10^{-2}N; 20°		Malic acid: $21·25 \times 10^{-2}$N; $Ce(SO_4)_2$: 10^{-2}N; 25°	
$[H_2SO_4]$ (N)	10^2k_s	$[H_2SO_4]$ (N)	10^2k_s	$[H_2SO_4]$ (N)	10^2k_s
0·50	46·2	1·00	1442	0·5	270
0·60	34·1	1·25	983	0·6	212·5
0·75	23·05	1·50	622	0·75	132·5
0·78	20·6	1·75	445	1·00	77·6
1·00	14·3	2·00	339	1·25	52·3
1·25	8·85	2·25	266·5		
1·50	6·4	2·50	203·5		

TABLE 3. *Effect of added salts on k_s (in* l. g.-equiv.$^{-1}$ min.$^{-1}$) for oxidation of organic acids.

Lactic acid: $5·75 \times 10^{-2}$N; $Ce(SO_4)_2$: 10^{-2}N; H_2SO_4: 0·6N; 25°			Mandelic acid: 10^{-2}N; $Ce(SO_4)_2$: 10^{-2}N; H_2SO_4: 2·0N; 20°			Malic acid: $21·25 \times 10^{-2}$N; $Ce(SO_4)_2$: 10^{-2}N; H_2SO_4: 0·75N; 25°		
[Salt] (M)		10^2k_s	[Salt] (M)		10^2k_s	[Salt] (M)		10^2k_s
K_2SO_4	0·02	30·1	$(NH_4)_2SO_4$	0·02	285	$(NH_4)_2SO_4$ ...	0·05	99·7
	0·04	25·5		0·04	270		0·10	79
	0·06	21·3		0·05	260		0·13	68·0
	0·08	18·2		0·08	230·5	$KHSO_4$	0·05	94·6
	0·10	15·9	$KHSO_4$	0·02	314		0·10	73·7
$KHSO_4$	0·04	32·9		0·04	296		0·15	52·5
	0·08	31·3		0·08	247			
				0·10	230			

(Fig. 2, Table 2). However, addition of an acid other than sulphuric acid (nitric or hydrochloric) produces only an insignificant retardation. Thus the main inhibitory ion is probably HSO_4^-.

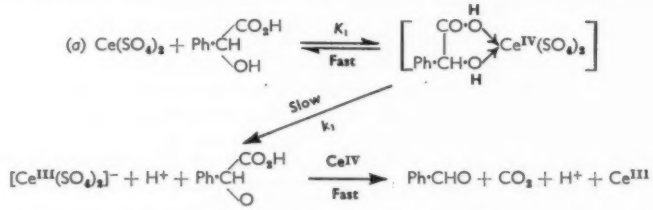
Potassium hydrogen sulphate, potassium sulphate, and ammonium sulphate produce significant retardations (see Table 3), though not according to any mathematical regularity.

The retardation produced by SO_4^{2-} ions might well be due to the formation of HSO_4^- ions by union with hydrogen ions from the sulphuric acid; the results for hydrogen sulphate or sulphate ions have only qualitative significance.

Salt Effect.—Addition of potassium chloride or nitrate also produces retardation, though not to the same extent as does sulphate or hydrogen sulphate ion. On the other hand, addition of sodium nitrate produces no retardation. We are thus not dealing here with the usual kinetic effect: the nature of the present salt effect is not clear.

Discussion

The reaction mechanism suggested here is based on Waters's theory [5] for the oxidation of α-hydroxy-acids by manganic pyrophosphate. Ceric sulphate and the organic hydroxy-acids (mandelic, DL-malic, or lactic acid) react rapidly to form an activated complex which then decomposes slowly to form a free radical, hydrogen ion, and cerous complex. The free radical takes up further cerium(IV) and by fast steps forms the rest of the reaction products. This is best illustrated in case of mandelic acid, where the mechanism is clear:



The presence of benzaldehyde and carbon dioxide was confirmed by the usual tests. The antocatalytic activity of HSO_4^- ion is explained by assuming that the reactive ceric salt species, $Ce(SO)_4)_2$, is removed by the following reactions:

$$(b)\ Ce(SO_4)_2 + HSO_4^- \overset{K_2}{\rightleftharpoons} HCe(SO_4)_3^-$$

$$(c)\ HCe(SO_4)_3^- + HSO_4^- \overset{K_3}{\rightleftharpoons} H_2Ce(SO_4)_4^{2-}$$

Taking into account the reaction schemes (*a*), (*b*), and (*c*) we then obtain:

$$-\frac{d[Ce^{IV}]}{dt} = \frac{k_1}{K_2K_3} \times \frac{[H_2Ce(SO_4)_4^{2-}][\text{Mandelic acid}]}{[HSO_4^-]^2} \qquad (1)$$

If various forms of ceric salt are held in rapid equilibrium (see below) the concentration of $H_2Ce(SO_4)_4^{2-}$ ion will be proportional to the total Ce^{IV} present in the reaction mixture. Hence eqn. (1) can be written in the form:

$$-d[Ce^{IV}]/dt = k_s'[Ce^{IV}][\text{Mandelic acid}]/[H_2SO_4]^2, \qquad (2)$$

where k_s' is another rate constant. For any given concentration of sulphuric acid eqn. (2) can be written in the form:

$$-d[Ce^{IV}]/dt = k_s[Ce^{IV}][\text{Organic acid}]$$

where k_s is the second-order constant determined experimentally.

The mechanism formulated explains the results observed for mandelic acid and ceric sulphate. With lactic acid the activated complex is of the same type. In the oxidation of lactic acid 5·75 equivalents of ceric sulphate are used and 0·3 mole of formic acid is

[5] Levesley and Waters, *J.*, 1955, 217.

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produced for each mole of lactic acid oxidised. The amount of formic acid produced was estimated by standard methods.[4,6] Carbon dioxide is also evolved. We thus assume that lactic acid is oxidised in two ways:

$$(d)\ Me{\cdot}CH(OH){\cdot}CO_2H + 10Ce^{IV} + 3H_2O \longrightarrow H{\cdot}CO_2H + 2CO_2 + 10H^+ + 10Ce^{III}$$
$$(e)\ Me{\cdot}CH(OH){\cdot}CO_2H + 4Ce^{IV} + H_2O \longrightarrow AcOH + CO_2 + 4H^+ + 4Ce^{III}$$

About 30% of the lactic acid undergoes reaction (*d*), and 70% reaction (*e*); this requires 5·8 equivalents of ceric sulphate and 0·3 mole of formic acid, very nearly as required. Both for lactic acid and for DL-malic acid it is difficult to visualize the actual course of the decomposition of the free radical, but since the kinetics of oxidation of both these acids is similar to that of mandelic acid one may assume that these oxidations proceed in a general way as follows:

$$Ce(SO_4)_2 + \alpha\text{-Hydroxy-acid} \underset{}{\overset{\text{Fast}}{\rightleftharpoons}} [\text{Activated complex}] \xrightarrow{\text{Slow}}$$
$$H^+ + Ce(SO_4)_2 + \text{Organic free radical} \xrightarrow{\text{Fast}} \text{Products}$$

In aqueous solutions of ceric sulphate containing sulphuric acid, a variety of complex ions is known to exist.[7] Depending on concentrations of sulphate and hydrogen ions, the composition of these solutions is believed to be governed by equilibria such as the following:

$$Ce(SO_4)_2 \rightleftharpoons Ce(SO_4)^{2+} + SO_4^{2-}$$
$$Ce(SO_4)_2 + SO_4^{2-} \rightleftharpoons Ce(SO_4)_3^{2-}$$
$$Ce(SO_4)_2 + HSO_4^- \rightleftharpoons HCe(SO_4)_3^- \rightleftharpoons Ce(SO_4)_3^{2-} + H^+$$
$$HCe(SO_4)_3^- + HSO_4^- \rightleftharpoons H_2Ce(SO_4)_4^{2-} \rightleftharpoons Ce(SO_4)_4^{4-} + 2H^+$$

If the species $Ce(SO_4)_2$ is the oxidant, the inhibiting effect of HSO_4^- ions then arises because these ions compete with the organic hydroxy-acids as ligands for cerium.

CHEMISTRY DEPARTMENT, UNIVERSITY OF ALLAHABAD,
ALLAHABAD, INDIA.

[*Received, November 7th*, 1960.]

[6] Vogel, " Text Book of Quantitative Inorganic Analysis," Longmans, Green & Co., London, 1953, p. 289.
[7] Moore and Anderson, *J. Amer. Chem. Soc.*, 1944, **66**, 1476; King and Pandou, *ibid.*, 1953, **75**, 3063; Hargreaves and Sutcliffe, *Trans. Faraday Soc.*, 1955, **51**, 1105; Hardwick and Robertson, *Canad. J. Chem.*, 1951, **29**, 828.

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594. *The Activity Coefficients of Aqueous Solutions of Choline Chloride at 25°.*

By R. FLEMING.

The isopiestic method has been used to determine the activity coefficients of aqueous solutions of choline chloride over the concentration range 0·1—4 molal. Fitting Robinson and Stokes's two-parameter equation to the experimental results requires a value of $\dot{a} = 3{\cdot}08$ and a hydration number of 2·65. Senko has found that the distance of closest approach between the choline and chlorine atoms in the crystal state is 3·04 Å.

THE activity coefficients of aqueous choline chloride solutions being important for another research we have determined them by the isopiestic method and have calculated the hydration number and distance of closest approach of the ions.

EXPERIMENTAL

The isopiestic apparatus was based on Robinson and Sinclair's design.[1] It consisted of four stainless-steel crucibles, each with a rhodium-plated hinged lid, and they rested on a circular

[1] Robinson and Sinclair, *J. Amer. Chem. Soc.*, 1934, **56**, 1830.

piece of brass, 1″ thick and 6″ in diameter. This ensured a good thermal contact between the crucibles. The brass plate, the crucibles, and the mechanism that operated the lids, were housed in a vacuum-desiccator inside a pivoted metal can, and the can was placed in a thermostat bath at 25° ± 0·01° kept in a cupboard at 25° ± 1°. Turning the tap of the desiccator opened or closed the lids of the crucibles. The can was rocked with a cam-mechanism and this caused glass balls placed in the crucibles to move, preventing the formation of diffusion gradients.

" AnalaR " potassium chloride, used as the reference substance, was dried at 110° for several hours before use. Choline chloride (B.D.H.) was purified by recrystallisation from absolute ethanol and its purity was checked by methods previously described.[2]

TABLE 1. *Isopiestic ratios.*

m_B	m_C	R	m_B	m_C	R	m_B	m_C	R
0·2000	0·1975	1·013	1·000	0·9606	1·041	1·600	1·510	1·060
0·4000	0·3923	1·020	1·200	1·145	1·048	1·800	1·690	1·065
0·6000	0·5842	1·027	1·400	1·328	1·054	2·000	1·868	1·071
0·8000	0·7737	1·034						

Two crucibles were used for the potassium chloride; the remaining two contained choline chloride. The required amount of substance was weighed into each crucible, triply distilled water was added, and the crucibles were placed in the apparatus which was then evacuated (water-pump) until the pressure was 10—12 mm. The apparatus was allowed to remain undisturbed for 3—7 days depending on the concentration of the solutions. Then the crucibles were reweighed and the concentrations of the solutions were calculated.

Results.—The apparatus was checked by determining the isopiestic ratio of potassium and sodium chloride solutions. The values obtained agree closely with those given by Robinson and Sinclair.[1] The results are shown in Table 1 where m_B and m_C are the molalities of potassium and sodium chloride respectively and R is the isopiestic ratio (m_B/m_C).

Experimental results for choline chloride, obtained with potassium chloride as reference substance, are shown in Table 2; they represent the summation of 3 runs over the concentration

TABLE 2. *Activity coefficient, γ_C, of choline chloride.*

m_B	m_C	R	ϕ_C	γ_C	γ_C (calc. $n = 2·65$, $\dot{a} = 3·08$)	m_B	m_C	R	ϕ_C	γ_C	γ_C (calc. $n = 2·65$, $\dot{a} = 3·08$)
0·1	0·1002	0·998	0·9247	0·769	0·759	1·4	1·410	0·992	0·8938	0·572	0·574
0·2	0·2005	0·997	0·9103	0·714	0·704	1·6	1·610	0·994	0·8988	0·567	0·570
0·3	0·301	0·996	0·9027	0·682	0·672	1·8	1·806	0·997	0·9054	0·564	0·567
0·4	0·402	0·995	0·8972	0·659	0·650	2·0	2·000	1·000	0·9124	0·563	0·565
0·5	0·503	0·994	0·8935	0·641	0·633	2·4	2·390	1·004	0·9251	0·562	0·564
0·6	0·605	0·992	0·8904	0·626	0·620	2·8	2·780	1·007	0·9380	0·564	0·566
0·7	0·707	0·990	0·8880	0·614	0·610	3·0	2·967	1·011	0·9470	0·567	0·568
0·8	0·809	0·988	0·8862	0·604	0·602	3·4	3·330	1·021	0·9676	0·576	0·573
0·9	0·910	0·989	0·8872	0·596	0·595	3·8	3·693	1·029	0·9866	0·585	0·579
1·0	1·010	0·990	0·8884	0·590	0·591	4·0	3·878	1·032	0·9956	0·590	0·583
1·2	1·210	0·991	0·8905	0·580	0·580						

range studied. In this Table, m_B is the molality of potassium chloride and m_C is the molality of choline chloride. R is the isopiestic ratio (m_B/m_C) and ϕ_C is the osmotic coefficient of the choline chloride calculated according to the equation $\phi_C = R\phi_B$. Values of ϕ_B for potassium chloride were taken from Appendix 8.3 of Robinson and Stokes's [3] book. The column γ_C shows the experimental value of the activity coefficient of choline chloride, c, calculated according to the equation: [1]

$$\ln \gamma_C = \ln \gamma_B + \ln R + \int_0^{m_B} (R - 1)\mathrm{d} \ln \gamma_B m_B.$$

The last term was evaluated graphically by using the equivalent form $2\int[(R - 1)/\sqrt{a_B}].\mathrm{d}\sqrt{a_B}$, $(R - 1)/\sqrt{a_B}$ being plotted against $\sqrt{a_B}$. The curve was extrapolated to zero concentration.

[2] Fleming, *J.*, 1960, 4914.
[3] Robinson and Stokes, " Electrolyte Solutions," Butterworths Scientific Publications, London, 1st edn., 1955, p. 461.

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Values for the activity of potassium chloride were obtained from Robinson and Stokes (Appendix 8.3).[3]

The calculated activity coefficients were obtained from Stokes and Robinson's two-parameter equation:[4]

$$\log \gamma_{\mathrm{C}} = -\frac{A|Z_1Z_2|\sqrt{I}}{1 + Ba\sqrt{I}} - \frac{n}{\nu}\log a_{\mathrm{A}} - \log\,[1 + 0{\cdot}001W_{\mathrm{A}}(\nu - n)m].$$

The second term was taken to be equivalent to $0{\cdot}007824 \times m \times \phi_{\mathrm{C}} \times n$ where n is the hydration number. It was found that values of the parameters $a = 3{\cdot}08$ and $n = 2{\cdot}65$ gave activity coefficients best fitting the experimental values. In the above equation $A = 0{\cdot}5092$, $W_{\mathrm{A}} = 0{\cdot}018$, and B was taken to be $0{\cdot}3286 \times 10^8$.

Discussion

Varimbi and Fuoss[5] have recently measured the conductance of choline iodide in dilute solution (0·001—0·021M) and have found that this salt shows no evidence of hydrogen bonding between the solvent molecules and the hydroxy-groups. These workers have found that the closest distance of approach between the choline and iodide ions is 5·39 Å ($3{\cdot}19 = r_+$) and that there is little evidence of ionic association. If it is assumed that

Table 3. *Calculations.* (*n and å refer to the two-parameter equations*).

m	Expt.	$n = 0$ $å = 3{\cdot}85$	$n = 2{\cdot}65$ $å = 4{\cdot}52$	$n = 3{\cdot}65$ $å = 3{\cdot}08$
0·503	0·641	0·645	0·686	0·633
1·010	0·590	0·595	0·595	0·591
2·000	0·563	0·552	0·552	0·565
2·967	0·567	0·530	0·530	0·568
3·878	0·590	0·516	0·516	0·583

there is no ion association in the more concentrated solutions used in this work, then it is possible to use Stokes and Robinson's two-parameter equation to calculate theoretical activity coefficients which will match the experimental values. The values of a and n required to give a close fit are 3·08 and 2·65 respectively, and the distance 3·08 Å seems too small, especially in view of the closest distance of approach found by Varimbi and Fuoss. Senko[6] has found that in the crystal state the distance between the chloride ion and oxygen atom is 3·04 Å and it appears that in concentrated solutions the distance between the choline and chlorine ions approaches that in the crystal state, although of course this is not the distance of closest approach between the ionic centres, as the oxygen atom is at the periphery of the choline ion.

An attempt was made to use the one-parameter equation of Robinson and Stokes:[7]

$$\log \gamma_1 = \frac{0{\cdot}5092|Z_1Z_2|\sqrt{I}}{1 + 0{\cdot}3286\sqrt{I}(\frac{3}{4}\pi(30n + V_1)^{\frac{1}{3}} + r_2 - \Delta)} - \frac{n}{\nu}\log A_{\mathrm{W}} - \log\,[1 - 0{\cdot}018\,(n - \nu)m]$$

where n is the hydration number, V_1 is the apparent molal volume of the ion in Å^3, and $\Delta = 0{\cdot}7$ represents "penetration distance." V_1 was estimated by using the relation $V_1 = V_{\mathrm{app}} - 6{\cdot}47Z_1r_2^3$ where V_{app} was taken as 124·1 c.c. and the radius of chloride ion r_2 was taken as 1·81 Å. Activity coefficients were first calculated by assuming that $n = 0$ ($å = 3{\cdot}85$ Å), and then with $n = 2{\cdot}65$ ($å = 4{\cdot}52$). The results are summarised in Table 3. They show that only the two-parameter equation fits the experimental results satisfactorily.

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Department of Physical Chemistry, School of Pharmacy, University of London, 29/39, Brunswick Square, London, W.C.1. [*Received, December 8th*, 1960.]

[4] Stokes and Robinson, *J. Amer. Chem. Soc.*, 1948, **70**, 1870.
[5] Varimbi and Fuoss, *J. Phys. Chem.*, 1960, **64**, 1335.
[6] Senko, U.S. Atomic Energy Comm. Report, 1957, U.C.R.L. 3521.
[7] Robinson and Stokes, ref. 3, p. 249.

595. *Chemical and Spectroscopic Evidence for the Occurrence of π-Character in Carbon–Boron Bonds.*

By T. D. Coyle, S. L. Stafford, and F. G. A. Stone.

Many organoboron compounds possess properties which suggest the presence in these compounds of carbon–boron π-bonding. This is discussed, and additional spectroscopic evidence is presented.

π-Bonding between carbon and boron has frequently been postulated to explain the properties of certain organoboron compounds. αβ-Unsaturated boronic esters and acids, for example, possess chemical and spectral properties strongly suggesting such bonding, a hypothesis in this instance supported by simple molecular orbital calculations.[1] We now supply additional experimental evidence for carbon–boron π-bonding, and discuss some earlier postulates of this bonding.

Evidence from Chemical Behaviour.—Carbon tetrachloride adds to dibutyl vinylboronate to form dibutyl 1,3,3,3-tetrachloropropylboronate; the low value for the first transfer constant ($3{\cdot}3 \pm 0{\cdot}7 \times 10^{-3}$) [1] is as expected if the intermediate radical is stabilized by electron delocalization involving the carbon–boron π-bonding, *viz.*,

$$CCl_3{\cdot}CH_2{\cdot}\dot{C}H{\cdot}B(OBu)_2 \longleftrightarrow CCl_3{\cdot}CH_2{\cdot}\overset{+}{C}H{\cdot}\bar{B}(OBu)_2$$

The relative stability towards disproportionation of vinyl- and propenyl-alkylboron compounds provides further chemical evidence for carbon–boron π-bonding.[2] Unless steric effects are a determining factor, as in large and branched-chain alkyl groups, unsymmetrical triorganoboron compounds (*e.g.*, BMe_2Et) are believed to have only a transient existence at ambient temperatures, disproportionating into the symmetrical triorganoboron compounds. These disproportionations undoubtedly proceed *via* a four-centre mechanism involving the p_π-orbital of boron. Clearly, if this p_π-orbital is involved in internal dative bonding, as is believed to occur in alkoxy- and amino-boranes and might occur in alkenylalkylboron compounds,[2] the tendency of the boron compound to disproportionate will be greatly reduced. Ritter and his co-workers [2] found that dimethylvinylborane decomposes only to the extent of about 33% after storage at room temperature for about 5 days. Similarly, methyldivinylborane can be heated to 100° for short periods without significant decomposition. The stability of these unsymmetrical boron compounds contrasts with the transient existence of such species as $BMeEt_2$, supporting the suggestion that mesomerism in alkenylboron derivatives restricts the boron atoms to a planar configuration and therefore inhibits disproportionation.

The stability of the perfluorovinylboron compounds is also interesting.[3] These are the first covalent organoboron compounds to contain a fully fluorinated organic group bonded to boron. Organoboron compounds having halogen atoms in the organic groups tend to decompose to form boron trihalides. Thus fluoromethylboron difluoride readily yields boron trifluoride,[4] and although 2-chloroethylboron compounds have not yet been obtained pure there is clear evidence that they are unstable.[5] It has long been held that a boron compound in which a highly fluorinated organic group is attached to boron would tend to decompose with formation of substances having boron–fluorine bonds. Thus, reaction between bispentafluoroethylmercury and boron trichloride affords boron trifluoride, and no compound containing a perfluoroalkyl–boron group is obtained by this

[1] Matteson, *J. Amer. Chem. Soc.*, 1960, **82**, 4228.
[2] Parsons and Ritter, *J. Amer. Chem. Soc.*, 1954, **76**, 1710; Parsons, Silverman, and Ritter, *ibid.*, 1957, **79**, 5091.
[3] Stafford and Stone, *J. Amer. Chem. Soc.*, 1960, **82**, 6238.
[4] Goubeau and Rohwedder, *Annalen*, 1957, **604**, 168.
[5] Hawthorne and Dupont, *J. Amer. Chem. Soc.*, 1958, **80**, 5830.

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method.[6,7] The behaviour of the perfluorovinylboron compounds is, however, significant. The dichloride is stable for short periods at 100° and at room temperature for several days before boron trifluoride is detected. Similarly, gaseous triperfluorovinylboron is stable for several days at room temperatures. The perfluorovinylboron compounds may owe their relatively high stability, compared with that of halogenoalkylboron compounds, to a contribution of the π-electrons of the perfluorovinyl group to the p_π-orbital of the boron atom, thereby inhibiting fluorine shift from the side chain to boron.

Further chemical evidence for carbon–boron π-bonding comes from the reduced electrophilic character of boron in certain compounds. In alkylboron halides there is a marked increase in pyrophoric character with branching of the alkyl groups. Steric and inductive factors suggest that reaction with oxygen would be faster for straight-chain than for branched-chain alkyl compounds. It has been suggested [8] that in the straight-chain compounds the boron atom's electrophilic character is reduced by contributions of resonance forms of the type $R\overset{+}{C}H_2{:}\overset{-}{B}Cl_2$. Delocalization of the vinyl groups' electrons into the boron p_π-orbital has been suggested to explain the absence of reaction between trivinylboron and oxygen at room temperature whereas under similar conditions triethylboron is rapidly consumed.[2] Carbon–boron π-bonding may also determine the properties of trimethylboron. Application of molecular-orbital theory to the electronic structure of trimethylboron leads to the conclusion [9] that exceptionally strong trigonal hyperconjugation stabilizes this molecule, and is responsible for trimethylboron's existing as a monomer rather than as the dimer, analogous to hexamethyldialuminium. There is an important distinction between the "hyperconjugation" postulated [9] for trimethylboron and that of organic chemistry. The σ-bonds in trimethylboron would have a charge separation $^-C{-}B^+$ of a magnitude not usually encountered in C–C bonds. Drift of electron density toward the boron p_π-orbital from the *pseudo*-p_π-orbitals which can be formed from the hydrogen atoms [10] of trimethylboron would lower the energy of the molecule not only by delocalization, but also by partial neutralization of the charge separations in the σ-bonds.

Exceptionally strong hyperconjugation in trimethylboron would tend to reduce the ability of the molecule to function as a Lewis acid, as is found experimentally: towards trimethylamine as reference base, Lewis acidity decreases in the sequence $Me_3Al > Me_3Ga > Me_3In > Me_3B > Me_3Tl$.[11] This sequence, except for the position of boron, perhaps reflects to some degree a decreasing tendency on the part of metals to accept partial negative charge with increasing electropositive character. Undoubtedly the position of boron in the order of acceptor power is due in part to steric factors.[12] Steric interference between groups on the donor and those on the acceptor in addition compounds $Me_3N{\cdot}M^{III}Me_3$ would be at a maximum when M^{III} is the smallest element of the group, the $N{-}M^{III}$ bond length then a minimum. Even if steric effects were negligible, however, it is doubtful [12] if trimethylboron would be a stronger acid than trimethylgallium. In the light of the molecular-orbital treatment of the bonding in trimethylboron [9] it seems reasonable to assume that part of the weakness of trimethylboron as an acid lies in the relatively large reorganizational energy [12] required in passing from the free acid, trimethylboron, to an adduct such as $Me_3N{,}BMe_3$. In trimethyl-aluminium and -gallium, as monomers, stabilization by π-bonding would be low, if current views on the inability of heavy atoms to form π-bonds by using p_π-orbitals are correct, so that relatively less adjustment energy is required in rehybridization of the acceptor atoms from sp^2 in the acids to the near sp^3-configuration in the adducts.

[6] Kaesz, Phillips, and Stone, *J. Amer. Chem. Soc.*, 1960, **82**, 6228.
[7] Lagowski and Thompson, *Proc. Chem. Soc.*, 1959, 301.
[8] McCusker, Ashby, and Makowski, *J. Amer. Chem. Soc.*, 1957, **79**, 5182.
[9] Mulliken, *Chem. Rev.*, 1947, **41**, 207.
[10] Coulson, *Quart. Rev.*, 1947, **1**, 144.
[11] Coates and Whitcombe, *J.*, 1956, 3351.
[12] Stone, *Chem. Rev.*, 1958, **58**, 101.

Further experimental support for π-bonding in trimethylboron comes from the fact that the equilibrium constant for the reaction $(CD_3)_3B_{(g)} + Me_3N_{(g)} = Me_3N,B(CD_3)_{3(g)}$ is greater than for the analogous reaction involving Me_3B.[13] Ready formation of the heavy addition compound $Me_3N,B(CD_3)_3$ is in agreement with the expectation that replacement of hydrogen atoms in trimethylboron by deuterium would lead to reduction of hyperconjugation with resultant increase in Lewis acidity.

Carbon–boron π-bonding also appears to influence the Lewis acidity of vinylboron difluoride. The gas-phase enthalpies of dissociation of the two addition compounds $Me_3N,BEtF_2$ and $Me_3N,BF_2{\cdot}CH{:}CH_2$ are not detectably different.[14] σ* values for organic groups bonded to boron indicate that the difference in electron-attracting power between a vinyl and an ethyl group in a compound RBF_2 should be sufficient to cause a measurable difference in Lewis acidity—the vinyl compound being the stronger electron-pair acceptor.[15] The observed equal acidity of the two organoboron fluorides strongly suggests that in vinylboron difluoride the expected inductive effect of the vinyl group is offset by some other factor, the most plausible being delocalization of π-electrons of the vinyl group into the boron p_π-orbital. This idea is supported by fluorine-19 nuclear magnetic resonance studies described below.

Evidence from Spectroscopic Studies.—The presence of conjugation in αβ-unsaturated organoboron compounds is suggested by both the position and the relative intensity of the C=C stretching band in the infrared spectra. Absorption frequencies for the C=C stretching band in unsaturated boron compounds are recorded in Table 1. Typical behaviour of a non-conjugated carbon–carbon double bond is illustrated by allylboron difluoride, in which the C=C stretching band occurs at 1650 cm.$^{-1}$, since the intermediate methylene group prevents conjugation. The corresponding band in αβ-unsaturated organoboron compounds, with the exception of the perfluorovinyl compounds, lies in the region 1630—1605 cm.$^{-1}$. This shift, considered together with the greater intensity of the band in these compounds compared to that in allylboron difluoride, provides strong evidence that these double bonds are conjugated with a group which removes electrons by π-delocalization.[16]

Additional evidence for conjugation in the vinylboron halides comes from consideration of the positions and intensities of the C=C stretching band in the spectra of the compounds $CH_2{:}CH{\cdot}BCl_2$ and $Me_3N,BCl_2{\cdot}CH{:}CH_2$. In the addition compound, boron does not possess a vacant orbital to accept π-electrons from the vinyl group, and therefore C=C stretching in this compound should show a weaker absorption at higher frequency than the corresponding peak in vinylboron dichloride, if delocalization occurs in the latter. Comparison of solutions in dichloromethane, at the same concentration, shows a shift of the double-bond absorption from 1599 cm.$^{-1}$ in the halide to 1613 cm.$^{-1}$ in the adduct and a decrease in intensity from 80% to 35% absorption.

In perfluorovinylboron compounds, the C=C stretching band occurs at higher frequencies than in the ordinary αβ-unsaturated boron compounds. This is as expected since the C=C stretching frequency increases when fluorine atoms are attached to carbon atoms forming the double bond.[17] For example, the C=C absorption changes from 1647 cm.$^{-1}$ in propene to 1767—1792 cm.$^{-1}$ in the fluoroethylenes. However, the C=C stretching band in perfluorovinylborons occurs at a significantly lower frequency than in normal fluoroalkenes, as would be expected if delocalization of the double-bond π-electrons into the boron p_π-orbital occurs. In this case again, formation of a trimethylamine adduct causes a shift to higher frequency of the C=C absorption (Table 1) as the possibility of overlap is destroyed.

[13] Love, Taft, and Wartik, *Tetrahedron*, 1959, **5**, 116.
[14] Coyle and Stone, *J. Amer. Chem. Soc.*, 1960, **82**, 6223.
[15] Kaesz and Stone. Amer. Chem. Soc. Monograph, "Organometallic Chemistry" (Ed. Zeiss), Reinhold, 1960, (Ch. 3).
[16] Bellamy, "The Infra-red Spectra of Complex Molecules," Wiley, New York, 2nd end., 1958.
[17] Torkington and Thompson, *Trans. Faraday Soc.*, 1945, **41**, 236.

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The C=C stretching band in perfluorovinylboron difluoride occurs at a higher frequency than in any other perfluorovinylboron compound and a similar relation holds for the C=C stretching band of vinylboron difluoride, compared to that of the other vinylboron halides. If the argument based on correlation of position of the C=C band with electron delocalization is correct, this suggests that carbon–boron π-bonding in perfluorovinyl- and vinyl-boron difluoride is less significant than in other vinylboron and perfluorovinylboron compounds listed in Table 1. As discussed below, fluorine-19 and boron-11 nuclear magnetic resonance studies also indicate that there is less carbon–boron π-bonding in organoboron fluorides. Presumably the boron p_π-orbital in the two difluorides is partially filled by p_π-electrons from the fluorine atoms of the BF_2 group, so that contribution of π-electron density from the unsaturated group to boron is less necessary to relieve electronic unsaturation at the boron atom. Nuclear magnetic resonance studies [18] can also be interpreted as indicating that fluorine atoms are more effective than chlorine atoms in π-bonding to boron, again implying that the relative contribution by the vinyl group of π-electron density to the vacant boron orbital would be less in the vinylboron fluorides than in the chlorides.

TABLE 1. C=C *Stretching bands in some unsaturated organoboron compounds.*

Compound	C=C stretch (cm.$^{-1}$)	Compound	C=C stretch (cm.$^{-1}$)	Compound	C=C stretch (cm.$^{-1}$)
$CH_2{:}CH{\cdot}CH_2{\cdot}BF_2$ [a]	1650 [b]			$CF_2{:}CFBF_2$ [h]	1725 [b]
				$CF_2{:}CFBCl_2$ [h]	1695 [b]
$CH_2{:}CH{\cdot}B(OH)_2$ [c]	1605 [d]	$CH_2{:}CH{\cdot}B(OBu)_2$ [c]	1610 [e]	$Me_2N,BCl_2{\cdot}CF{:}CF_2$	1736
$CH_2{:}CMe{\cdot}B(OH)_2$ [c]	1615 [d]	$CH_2{:}CMe{\cdot}B(OBu)_2$ [c]	1625 [e]		
$CH_2{:}CHBF_2$ [a]	1629 [b]	$(CH_2{:}CH)_2BF$ [a]	1625 [b]	$(CF_2{:}CF)_2BCl$ [h]	1677 [b]
$CH_2{:}CHBCl_2$ [a]	1610,[b] 1599	$(CH_2{:}CH)_2BCl$ [a]	1612 [b]	$(CF_2{:}CF)_3B$ [h]	1678 [b]
$Me_2N,BCl_2{\cdot}CH{:}CH_2$	1613 [f,g]	$(CH_2{:}CH)_3B$ [a]	1610 [b]		

[a] Ref. 19. [b] Gas phase. [c] Ref. 1. [d] Chloroform solution. [e] Neat liquid. This work, methylene chloride solution. [f] Band is much weaker in complex. [h] Ref. 3.

The ultraviolet spectral properties of αβ-unsaturated organoboron compounds have also suggested resonance interaction between π-electrons of the carbon–carbon double bond and the p_π-orbital of an adjacent boron atom, *e.g.*, the observation by Letsinger and Skoog [20] of an absorption maximum at 223 mμ (ε 1000) in the spectrum of 2-methylprop-1-enylboronic acid. Neither alkenes nor alkylboronic acids absorb in this region.

We have examined the ultraviolet spectra of the vapours of the halides $Et{\cdot}BCl_2$, $CH_2{:}CH{\cdot}BCl_2$, $(CH_2{:}CH)_2BCl$, and $CH_2{:}CH{\cdot}BF_2$. Ethylboron dichloride and vinylboron difluoride exhibit only a weak " end absorption " down to 200 mμ, the spectra being rather similar to that of vinyl chloride. However, in vinylboron dichloride and divinylboron chloride there are maxima, at 207 mμ (ε ~7000) and 210 mμ (ε ~8000), respectively. The absence of a maximum in the spectrum of vinylboron difluoride suggests that the carbon–boron π-interaction is less significant than in the chloride: this agrees with the infrared and nuclear magnetic resonance results.

Studies of boron-11 chemical shifts [21,22] suggest that the magnitudes of the shifts are related, at least in part, to the degree to which the vacant *p*-orbital of the trigonal boron atom is occupied, being greatest in the extreme case of tetrahedrally-substituted boron. Values of some boron-11 chemical shifts we have obtained are given in Table 2.

The results show that in the dichlorides and the difluorides the boron atom is more shielded in the vinyl compound than in the ethyl derivative, as would be expected if π-bonding is the cause. In addition, the higher shifts for the fluorides, coupled with the

[18] Coyle and Stone, *J. Chem. Phys.*, 1960, **32**, 1892.
[19] Brinckman and Stone, *J. Amer. Chem. Soc.*, 1960, **82**, 6218.
[20] Letsinger and Skoog, *J. Org. Chem.*, 1953, **18**, 895.
[21] Onak, Landesman, Williams, and Shapiro, *J. Phys. Chem.*, 1959, **63**, 1533.
[22] Phillips, Miller, and Muetterties, *J. Amer. Chem. Soc.*, 1959, **81**, 4496.

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TABLE 2. *Boron-11 chemical shifts.*

Compound	Shift (p.p.m.) [a]	Compound	Shift (p.p.m.) [a]	Compound	Shift (p.p.m.) [a]	Compound	Shift (p.p.m.) [a]
$Et{\cdot}BCl_2$	−16·0	$CH_2{:}CH{\cdot}BCl_2$	−6·2	EtBClF	1·7	$CH_2{:}CH{\cdot}BF_2$	24·2
$Ph{\cdot}BCl_2$	−6·7 [b]	BCl_3	0	$EtBF_2$	18·9		

[a] BCl_3 as external reference. [b] Ref. 22.

smaller effect of substituting vinyl for ethyl in the fluorides, compared with the chlorides, also suggests that carbon–boron π-bonding is less significant in the fluorides. It is of interest that the chemical shift of phenylboron dichloride, for which dipole-moment measurements indicate strong resonance involving carbon–boron π-bonded structures,[23] is very close to that of vinylboron dichloride. However, the boron-11 chemical shifts of butyl- and phenyl-boronic acids differ by only 0·9 p.p.m.[22] Clearly, if carbon–boron π-bonding is a significant factor in these chemical shifts, its importance must vary considerably as the other substituents on the boron atom are varied.

The possibility of partial donation of lone-pair electrons from fluorine orbitals of suitable symmetry into the vacant *p*-orbital of boron in boron trifluoride has long been recognized [24] and is invoked to explain the observed weakness of boron trifluoride as a Lewis acid compared with boron trichloride and boron tribromide.[25] Such interactions would occur equally well in organoboron fluorides with the character of the B–F bonds differing in RBF_2 and $R'BF_2$ if R and R′ differ in π-bonding ability. It is assumed that fluorine-19 chemical shifts can be correlated with electron density at the fluorine atom, a hypothesis supported by theoretical work [26] and experimental data, and since organic groups in general should be poorer π-donors than fluorine, a withdrawal of electron density from the remaining fluorines would be expected when one fluorine atom in boron trifluoride is replaced by an organic group, even though the latter is usually considered to be less " electronegative." Fluorine-19 chemical shifts, summarized in Table 3, show that relative to boron trifluoride

TABLE 3. *Fluorine-19 chemical shifts*

Compound	Shift (p.p.m.) [a]	Compound	Shift (p.p.m.) [a]	Compound	Shift (p.p.m.) [a]
BF_3 [b]	0	$CH_2{:}CH{\cdot}CH_2{\cdot}BF_2$ [c]	−52	Me_2N,BF_2 [c]	+37
$Ph{\cdot}BF_2$ [c]	−35	Pr^nBF_2 [b]	−54	$Me_2N,BEtF_2$ [c]	+38
$CH_2{:}CH{\cdot}BF_2$ [b]	−38	$Bu{\cdot}BF_2$ [c]	−54	$Me_2N,BF_2{\cdot}CH{:}CH_2$	+39
$CF_2{:}CF{\cdot}BF_2$ [f]	−40	EtBClF [d]	−99		
$EtBF_2$ [b]	−52	Me_2BF [c]	−107		

[a] Chemical shifts were measured, unless otherwise stated, in dilute solution in CCl_3F, $\delta(BF_3) = 127$ p.p.m. relative to internal CCl_3F. Since minor variations can be expected with changes in solution conditions, etc., values are expressed to the nearest p.p.m. [b] Ref. 14. [c] J. P. Grivet, unpublished observations. [d] From shift relative to $EtBF_2$ in mixture of composition EtBClF, $\delta(EtBF_2)$ being taken as −52 p.p.m. [e] Measured in dilute CH_2Cl_2 solution, for which $\delta(BF_3)$ is taken as 127 p.p.m., relative to external CCl_3F. [f] BF_2 fluorine atoms.

there is indeed less magnetic shielding of the fluorine nuclei with displacement of the resonance to lower applied field in organoboron fluorides. The fluorine-19 chemical shifts of the alkylboron fluorides appear at somewhat lower applied field than those of vinylboron fluorides, perfluorovinylboron difluoride, or phenylboron difluoride, while in the trimethylamine adducts of ethyl- and vinyl-boron difluoride the chemical shifts are almost identical. This agrees with the concept of carbon–boron π-bonding when the carbon atom bonded to trigonal boron has a filled p_π-orbital, leading to the appearance of the fluorine-19 resonances at higher field than in alkylboron fluorides.

Fluorine-19 nuclear magnetic resonance studies of the perfluorovinyl derivatives of boron may also reveal π-interactions The chemical shifts of the fluorine atoms of the

[23] Curran, McCusker, and Makowski, *J. Amer. Chem. Soc.*, 1957, **79**, 5188.
[24] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, 3rd Ed., 1959, p. 318.
[25] Brown and Holmes, *J. Amer. Chem. Soc.*, 1956, **78**, 2173.
[26] Saika and Schlichter, *J. Chem. Phys.*, 1954, **22**, 26.

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difluoromethylene group in the boron halides $CF_2{:}CF{\cdot}BF_2$, $CF_2{:}CF{\cdot}BCl_2$, and $(CF_2{:}CF)_3B$ are substantially lower (73—76 p.p.m. and 88—100 p.p.m., respectively, for *trans*- and *cis*-fluorine atoms) than the corresponding shifts for perfluorovinyl derivatives of silicon, tin, arsenic, or mercury (83—90 and 112—125 p.p.m.).[27] Moreover, some F–F spin-coupling constants in perfluorovinyl groups bonded to boron depart markedly from the values obtained for other perfluorovinylmetals[27] or for fluoro-olefins in general.[28] It seems reasonable to infer that a rather unusual perturbation of the electron system of the perfluorovinyl group is characteristic of the boron derivatives.

Experimental

Infrared spectra were recorded as gases in a 4-cm. cell, or as solutions in a 0·4 mm. liquid cell, fitted with sodium chloride plates, a Perkin–Elmer Model 21 double-beam spectrometer being used with sodium chloride optics. Spectra were calibrated immediately against known peaks of a polystyrene film.

Ultraviolet spectra were obtained as gases in a 4-cm. cell fitted with quartz windows, a Cary model 11M recording spectrometer being used.

Nuclear magnetic resonance spectra were recorded at room temperature on a Varian V-4300B nuclear magnetic resonance spectrometer operating at 40 Mc./sec. for fluorine-19 and 15·1 Mc./sec. for boron-11.

The compounds studied were prepared as described in the references mentioned.

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The Mallinckrodt Chemical Laboratory,
Harvard University, Cambridge, Massachusetts. [*Received, December 13th*, 1960.]

[27] Coyle, Stafford, and Stone, *Spectrochim. Acta*, in the press.
[28] McConnell, Reilly, and McClean, *J. Chem. Phys.*, 1956, **24**, 479.

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596. *Homolytic Aromatic Substitution. Part XXIV.* The p-Methylphenylation of Nitrobenzene and Chlorobenzene.*

By J. K. Hambling, D. H. Hey, S. Orman, and Gareth H. Williams.

The determination, by means of competitive experiments, of the relative rates of *p*-methylphenylation of nitrobenzene and chlorobenzene is reported. The ratio of isomers formed in the *p*-methylphenylation of nitrobenzene is also determined. The results, which indicate that the *p*-methylphenyl radical is slightly nucleophilic in character, are consistent with the hypothesis that the permanent polarisation of the substituent has a small but significant influence on the properties of the free substituted aryl radical.

In Part XIX,[1] determinations were reported of the relative rates of arylation of nitrobenzene and chlorobenzene, with the electrophilic *p*-nitrophenyl and *p*-methoxyphenyl radicals, and of the proportions in which the *ortho*-, *meta*-, and *para*-isomers were formed in the *p*-nitrophenylation of nitrobenzene. These results, together with those reported in earlier papers in this series, were shown to be consistent with the hypothesis that a measure of electrophilic character is conferred on the radicals by virtue of the electron-attracting properties of the substituents present therein. It is, therefore, of interest to investigate the polar properties of radicals containing electron-repelling substituents, since these should, on the basis of the above-mentioned hypothesis, exhibit a measure of nucleophilic character, and the rates of attack by them on individual positions in aromatic nuclei,

* Part XXIII, *J.*, 1961, 565.
[1] Hambling, Hey, and Williams, *J.*, 1960, 3782.

when compared with the corresponding rates of attack by phenyl radicals, should exhibit changes in the opposite sense from those observed with electrophilic radicals. The present investigation is directed to the observation of such changes in the arylation of nitrobenzene and chlorobenzene with *p*-methylphenyl radicals. The relative rates of attack by these radicals on nitrobenzene and chlorobenzene, and the distribution of the isomeric biaryls formed in the *p*-methylphenylation of nitrobenzene, have therefore been measured. The results are shown to be consistent with the assumption of slight nucleophilic character by the *p*-methylphenyl radical.

Experimental

Reagents.—Solids were recrystallised to constant m. p. Benzene, chlorobenzene, and nitrobenzene were purified as described in Part II,[2] and *NN*-dimethylformamide as described in Part XIX.[1] *p*-Toluoyl peroxide was prepared by Swain, Stockmayer, and Clarke's method [3] and had m. p. 136° (decomp.).

4-Methyl-2′-nitrobiphenyl (m. p. 37°) was prepared by the reaction of diazotised *p*-toluidine with a stirred mixture of nitrobenzene and aqueous sodium hydroxide, Hey, Nechvatal, and Robinson's method [4] being used. The product was purified by chromatography on alumina and crystallisation from light petroleum (b. p. 60—80°). 4-Methyl-4′-nitrobiphenyl (m. p. 140°) was prepared by the nitration of 4-methylbiphenyl (Grieve and Hey's method [5]). 4-Methylbiphenyl (m. p. 49°) was prepared by Gomberg and Pernert's method.[6]

A specimen of 4-methyl-3′-nitrobiphenyl, originally prepared by the Hey, Nechvatal, and Robinson method,[4] was recrystallised from light petroleum (b. p. 60—80°) to m. p. 76·5°

Determination of $\frac{Ph\cdot NO_2}{PhH}K$ *for* p-*Methylphenylation.*—In experiments 1—4, *p*-toluoyl peroxide (6 g.) was allowed to decompose in a mixture of benzene (107·3 ml.) and nitrobenzene (92·3 ml.) in a thermostat at 80° for 72 hr. The mixed biaryls formed were isolated by a modification of the procedure described in Part XVIII,[7] each mixture being divided into two portions (A and B) before the final distillation. The modification of this procedure, which was introduced in order to prevent losses of the relatively volatile 4-methylbiphenyl, was that the bulk of the residual nitrobenzene solvent was distilled at a relatively high pressure (b. p. 140°/105 mm.). Before the final distillation the remaining nitrobenzene was removed at room temperature by maintaining the contents of the distillation flask at a pressure of 0·01 mm. for 12 hr., after which the flask was warmed to 35° to give the fore-run. The fore-runs were analysed by estimation of their content of nitro-group, and corrections in terms of methylbiphenyl were applied to the yield and composition of the biaryl fractions. Fractions taken immediately before the fore-runs were shown to consist entirely of nitrobenzene, showing that neither the fore-runs nor the biaryl fractions were contaminated with benzene, and that the whole of the 4-methylbiphenyl formed was contained in the fore-runs and the biaryl fractions. The absence of methylnitrobiphenyls from the fore-runs is inferred, since these compounds did not begin to distil until a temperature of 45° above that at which the fore-runs were collected had been reached. The biaryl fractions, the fore-runs, and the final fraction of the solvent were analysed volumetrically for nitro-groups by titration with titanous sulphate as described in Part XVIII.[7] The results of experiments 1—4 are given in Table 1.

Determination of $\frac{Ph\cdot NO_2}{PhCl}K$ *for* p-*Methylphenylation.*—In experiments 5 and 6, *p*-toluoyl peroxide (6 g.) was allowed to decompose in a mixture of chlorobenzene (99·3 ml.) and nitrobenzene (100·7 ml.) in a thermostat at 80° for 72 hr. The reactions were conducted, and the products isolated and analysed, as described in Part XIX [1] for the determination of this relative rate for arylation with other aryl radicals. Fore-runs were collected and analysed, and corrections in terms of chloromethylbiphenyls were applied to the weight and composition of the biaryl fractions. Fractions taken immediately before the fore-runs were shown to consist entirely of nitrobenzene. The absence of methylnitrobiphenyls from the fore-runs is assumed, since

[2] Augood, Hey, and Williams, *J.*, 1952, 2094.
[3] Swain, Stockmayer, and Clarke, *J. Amer. Chem. Soc.*, 1950, **72**, 5432.
[4] Hey, Nechvatal, and Robinson, *J.*, 1951, 2892.
[5] Grieve and Hey, *J.*, 1932, 1888.
[6] Gomberg and Pernert, *J. Amer. Chem. Soc.*, 1926, **48**, 1372.
[7] Hey, Moulden, and Williams, *J.*, 1960, 3769.

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these compounds did not begin to distil until a temperature 45° above that at which the fore-runs were collected had been reached. The results are given in Table 2.

TABLE 1.

	Expt. 1		Expt. 2		Expt. 3		Expt. 4	
	A	B	A	B	A	B	A	B
Biaryl fraction (b. p. 38—130°/0·015 mm.) (g.)	1·588	1·516	1·686	1·395	1·698	1·306	1·468	1·555
Nitrobiaryls in biaryl fraction (%)	82·6	82·9	82·9	82·2	82·6	82·9	82·9	82·2
Fore-run (b. p. 17—35°/0·01 mm.) (g.)	1·153	1·478	0·820	1·229	1·314	1·277	1·003	0·962
4-Methylbiphenyl in fore-run (g.)	0·013	0·021	0·011	0·010	0·054	0·060	0·029	0·042
Corr. wt. of biaryl fraction (g.)	1·601	1·537	1·697	1·405	1·752	1·366	1·497	1·597
Nitrobiaryls, corr. (%)	82·0	81·8	82·4	81·7	80·0	79·5	81·3	80·0
$^{Ph\cdot NO_2}_{PhH}K$ for *p*-methylphenylation	3·58	3·55	3·70	3·52	3·12	2·96	3·43	3·12
Residue (g.)	0·199		0·210		0·200		0·202	
Free *p*-toluic acid (g.)	2·80		2·76		2·70		2·64	
p-Toluic acid from hydrolysis of esters (g.)	0·34		0·35		0·34		0·35	
$(p\text{-}CH_3\cdot C_6H_4\cdot CO\cdot O)_2$ accounted for (%)	87·6		86·1		80·7		79·6	

Hence $^{Ph\cdot NO_2}_{PhH}K$ for *p*-methylphenylation = 3·4.

TABLE 2.

	Expt. 5	Expt. 6
Biaryl fraction (b. p. 40—128°/0·01 mm.) (g.)	3·291	3·371
Nitrobiaryls in biaryl fraction (%)	73·6	73·5
Fore-run (b. p. 25—40°/0·01 mm.) (g.)	2·020	1·105
Chloromethylbiphenyls in fore-run (g.)	0·068	0·047
Corr. wt. of biaryl fraction (g.)	3·359	3·418
Nitrobiaryls, corr. (%)	72·1	72·5
$^{Ph\cdot NO_2}_{PhCl}K$ for *p*-methylphenylation	2·48	2·52
Free *p*-toluic acid (g.)	2·60	2·65
p-Toluic acid from hydrolysis of esters (g.)	0·31	0·29
Residue (g.)	0·270	0·329
$(p\text{-}CH_3\cdot C_6H_4\cdot CO\cdot O)_2$ accounted for (%)	85·0	86·5

Hence $^{Ph\cdot NO_2}_{PhCl}K$ for *p*-methylphenylation = 2·5.

Determination of the Ratio of Isomerides formed in the p-*Methylphenylation of Nitrobenzene.*—In experiments 7 and 8, *p*-toluoyl peroxide (6 g.) was allowed to decompose in nitrobenzene (200 ml.) in a thermostat at 80° for 72 hr. The standard procedure (Part II [2]) was used for the isolation of the biaryl fractions, which were shown by analysis to contain no extraneous material. The yields of the various products obtained are given in Table 3.

TABLE 3.

	Expt. 7	Expt. 8
Biaryl fraction (b. p. <128°/0·01 mm.) (g.)	3·543	3·536
Free *p*-toluic acid (g.)	2·63	2·61
p-Toluic acid from hydrolysis of esters (g.)	0·41	0·34
Residue (g.)	0·394	0·294
p-Toluoyl peroxide accounted for (%)	92·5	91·0

TABLE 4. *Analysis of mixtures of* 4-*methylnitrobiphenyls.*

	Composition (%)		
Mixture	4,2′-	4,3′-	4,4′-
7	59·3	11·9	28·8
8	59·7	12·0	28·3
Mean	59·5	11·9	28·6
S (Found)	69·1	2·4	28·5
S (Known)	67·7	2·9	29·4

The mixtures of isomeric methylnitrobiphenyls were analysed by the infrared spectrographic method described in Part XIX.[1] The characteristic absorption bands used for the analysis were as follows: 4-methyl-2′-nitrobiphenyl, 787 cm.$^{-1}$; 4-methyl-3′-nitrobiphenyl, 744 cm.$^{-1}$. The amount of 4-methyl-4′-nitrobiphenyl present in the mixtures was obtained by difference. In order to check the accuracy of the analyses, a synthetic mixture (S) known composition was made up and analysed. The results of these analyses are given in Table 4.

Discussion

The relative rate of *p*-methylphenylation of nitrobenzene has been determined directly, while that of chlorobenzene may be calculated from the measured value of $^{Ph\cdot NO_2}_{PhCl}K$, since $^{Ph\cdot Cl}_{PhH}K = {}^{Ph\cdot NO_2}_{PhH}K / {}^{Ph\cdot NO_2}_{PhCl}K$. These results are given in Table 5, in which the relative rates of phenylation of nitrobenzene and chlorobenzene are included for comparison.

It is immediately obvious from these results that both aromatic compounds, which contain electron-attracting directing groups, are relatively more reactive towards *p*-methylphenyl than towards phenyl radicals. This is consistent with the hypothesis, outlined earlier, that the electron-repelling methyl group confers a measure of nucleophilic character

Table 5.

	$^{Ph\cdot NO_2}_{PhH}K$	$^{PhCl}_{PhH}K$
p-Methylphenylation	3·4	1·4
Phenylation [a]	2·9	1·1

Table 6. *Partial rate factors for arylation of nitrobenzene.*

	F_o	F_m	F_p
p-Methylphenylation	6·1	1·2	5·8
Phenylation	5·5	0·86	4·9

on the *p*-methylphenyl radical. This conclusion is also consistent with the values of the partial rate factors for *p*-methylphenylation of nitrobenzene, which may be calculated from the relative rate and isomer distribution for this reaction. These values are given in Table 6, together with the corresponding values for phenylation for comparison.

It may be noted that, although the polar influences involved are too weak to affect the isomer distribution to any appreciable extent (the differences are actually within the estimated experimental error of $\pm 2\%$), all the partial rate factors for *p*-methylphenylation are higher than those for phenylation, as would be expected on the basis of the above interpretation of the properties of substituted aryl radicals.

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King's College (University of London),
Strand, London, W.C.2.
Birkbeck College (University of London),
Malet Street, London, W.C.1.

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[a] Hey, Orman, and Williams, *J.*, 1961, 565.

597. *Homolytic Aromatic Substitution. Part XXV.* The Determination of the Total and Partial Rate Factors for the Phenylation of Naphthalene.*

By D. I. Davies, D. H. Hey, and Gareth H. Williams.

Benzoyl peroxide is shown to be unsuitable for the determination of the rate ratio in a competitive reaction with nitrobenzene and naphthalene. The rate of phenylation of naphthalene relative to that of nitrobenzene has been determined with phenyl radicals derived from *N*-nitrosoacetanilide. A value for $^{C_{10}H_8}_{C_6H_6}K$ has been derived, as also have the partial rate factors for phenylation at the 1- and the 2-position. The values thus obtained are discussed and compared with those derived from earlier work and from theoretical calculations.

The first attempt to determine the relative rate of the phenylation of naphthalene $^{C_{10}H_8}_{C_6H_6}K$ was reported by Huisgen and Sorge,[1] who used a competitive reaction in which the solvent was a mixture of benzene and naphthalene with *N*-nitrosoacetanilide as the source of the phenyl radical. They reported values ranging from 31 to 17·7 but, on account of the difficulty in eliminating or estimating losses of biphenyl during the removal of the excess of benzene and naphthalene these values are probably high. Hey and Williams subsequently reported [2] a value of 23·9, which was based on work carried out by Augood,[3] who used a competitive reaction between naphthalene and nitrobenzene with benzoyl peroxide as the source of the phenyl radical. This result cannot now be accepted because it has since been established [4] that the reaction between benzoyl peroxide and naphthalene is complicated by the formation of binaphthyls and appreciable quantities of esters. It was also reported [3] that aniline was isolated after hydrolysis of the product from the naphthalene–nitrobenzene reaction. A redetermination of $^{C_{10}H_8}_{C_6H_6}K$ was reported by Huisgen and Grashey [5] who used a competitive reaction with naphthalene and pyridine, *N*-nitrosoacetanilide again being used as the source of the phenyl radical. The values reported ranged from 13 to 8·3. More recently, Huisgen, Jakob, and Grashey [6] have reported competitive reactions with benzene and naphthalene, using phenylazotriphenylmethane, *N*-nitrosoacetanilide, and benzoyl peroxide as radical sources. In these determinations a more refined analytical technique was used which involved the use of isotopically labelled carbon. With phenylazotriphenylmethane and with *N*-nitrosoacetanilide values ranging from 13·5 to 14·7 were obtained, whereas with benzoyl peroxide the values were 10·5 and 11·5. The values 10·5 and 11·5 must again be distrusted because the reaction with benzoyl peroxide and naphthalene leads also to binaphthyls.

Experiments are now reported on competitive reactions with mixtures of naphthalene and nitrobenzene, in which *N*-nitrosoacetanilide was the source of the phenyl radical. These reactions gave a value of 9·9 for $^{C_{10}H_8}_{C_6H_6}K$. The formation of aniline in the hydrolysis products obtained in this reaction is also confirmed and discussed. These results have been reported briefly elsewhere.[7]

* Part XXIV, preceding paper.

[1] Huisgen and Sorge, *Annalen*, 1950, **566**, 162.
[2] Hey and Williams, *Discuss. Faraday Soc.*, 1952, **14**, 216.
[3] Augood, Ph.D. Thesis, University of London, 1952.
[4] Davies, Hey, and Williams, *J.*, 1958, 1878.
[5] Huisgen and Grashey, *Annalen*, 1957, **607**, 46.
[6] Huisgen, Jakob, and Grashey, *Ber.*, 1959, **92**, 2206.
[7] Hey, Kekulé Symp., "Theoretical Organic Chemistry," Butterworths Scientific Publ., London, 1959, 250.

Experimental

Reagents.—Benzoyl peroxide and nitrobenzene were purified as described in Part II [8] and naphthalene as described in Part XIII.[4] *N*-Nitrosoacetanilide was prepared by France, Heilbron, and Hey's method.[9]

Decomposition of Benzoyl Peroxide in a Mixture of Nitrobenzene and Naphthalene—Benzoyl peroxide (6 g.) was allowed to decompose in an equimolar mixture of nitrobenzene (97·9 g.) and naphthalene (102·1 g.) kept at 80° in a thermostat for 72 hr. The reaction was carried out in duplicate (Expts. 1 and 2). The resulting dark solutions, which partially solidified on standing, were worked up as in the benzoyl peroxide–naphthalene reactions described in Part XIII [4] except that benzene–light petroleum (b. p. 60—80°) (1 : 1) was used as eluent in the chromatographic stage in place of benzene. In addition, the benzene solution containing the biaryls, obtained after the hydrolysis of the esters, was repeatedly shaken with concentrated hydrochloric acid, which gave a deep purple extract. Neutralisation of this extract with aqueous sodium hydroxide gave an orange-coloured cloudy solution which was extracted with methylene chloride (3 × 40 ml.) and then with ether (40 ml.). The combined dark red extracts were dried (Na_2SO_4) and removal of the solvents by distillation at atmospheric pressure left a residue from which aniline distilled at 80°/20 mm. Its identity was established by infrared spectroscopy and preparation of its benzoyl derivative (m. p. and mixed m. p. 163°). The non-volatile red residue probably contained azobenzene. The main products isolated from these reactions are shown in Table 1.

Table 1. *Products from the decomposition of benzoyl peroxide in nitrobenzene–naphthalene.*

Expt. No.	1	2
Free benzoic acid (g.)	3·35	3·38
Benzoic acid from hydrolysis of esters and benzanilide (g.)	2·26	2·22
Biaryl fraction, b. p. 108—140°/0·1 mm. (g.)	1·14	1·17
Biaryl fraction, b. p. 150—180°/0·1 mm. (g.)	0·61	0·57
Residue after distillation of biaryls (g.)	0·08	0·06
Aniline (after hydrolysis) (g.)	0·49	0·52
Residue after distillation of aniline (g.)	0·15	0·21
Peroxide accounted for, calculated on the weights of free and ester acid (%)	92·7	92·6

The biaryl fraction, b. p. 108—140°/0·1 mm., contained 4·15% of nitrogen. If this fraction contains only nitrobiphenyls and phenylnaphthalenes its composition must be 59% of the former and 41% of the latter, but this would account for more than 100% of the peroxide. The fraction is most likely to contain, in addition, nitrophenylnaphthalenes because naphthyl radicals, generated by abstraction of hydrogen from naphthalene by benzoyloxy-radicals, can attack nitrobenzene (as well as naphthalene). Attempts to isolate single compounds from this fraction were unsuccessful. The second biaryl fraction (b. p. 150—180°/0·1 mm.) was dissolved in hot light petroleum (b. p. 80—100°) (20 ml.); when the solution was cold, 2,2′-binaphthyl (0·029 g.) separated in plates, m. p. and mixed m. p. 183—184°. Concentration of the mother-liquor gave crystals, m. p. 130—135°, the infrared spectrum of which was consistent with that required for a mixture of 1,1′- and 1,2′-binaphthyl.

In a third experiment it was found that after removal of the free acid from the benzene solution of the product by extraction with saturated aqueous sodium hydrogen carbonate, subsequent extraction with concentrated hydrochloric acid gave no aniline, which is therefore not a final product of the reaction.

Determination of $\frac{C_{10}H_8}{PhNO_2}$*K.*—*N*-Nitrosoacetanilide (5 g.) was added slowly during 1 hr. to a mixture of nitrobenzene (158·7 g.) and naphthalene (41·3 g.) (molar ratio 4 : 1) in a thermostat at 20°. The reaction was carried out in quadruplicate (Expts. 3—6). Nitrogen was steadily evolved and the colour of the solutions changed from yellow to red and finally to dark red. After 3 days the acetic acid and excess of nitrobenzene and naphthalene were removed by distillation at 20 mm. with a helix-packed column. The residue (*ca.* 25 ml.) was boiled under reflux for 4 hr. with a 1 : 1 mixture (100 ml.) of ethanol and concentrated hydrochloric acid.

[8] Augood, Hey, and Williams, *J.*, 1952, 2094.
[9] France, Heilbron, and Hey, *J.*, 1940, 369.

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The ethanol was then distilled off and the mixture was extracted with benzene (4 × 40 ml.). The benzene solution was successively washed with (*a*) concentrated hydrochloric acid (10 × 50 ml.), (*b*) 2N-aqueous sodium hydroxide (3 × 50 ml.), and (*c*) water (2 × 50 ml.). After the resulting solution had been dried ($CaCl_2$), most of the benzene was removed from it by distillation, and the residue (*ca.* 30 ml.) was subjected to chromatography on alumina (35 × 1·5 cm.). Elution was effected with a 1 : 1 mixture (500 ml.) of benzene and light petroleum (b. p. 60—80°). The pale orange-yellow eluate gave, on distillation, the biaryl fraction which was collected at 0·1 mm. The weights of the biaryls and non-volatile residues are shown in Table 2.

The biaryl fractions were estimated for nitro-group content by reduction with titanous sulphate by the method described in Part XVIII.[10] In the distillation of the biaryls a small forerun was rejected in order to ensure that the fraction submitted for analysis contains no nitrobenzene or naphthalene. The analytical results are also included in Table 2.

TABLE 2. *Weights of biaryls and residues obtained in the reaction of N-nitrosoacetanilide with nitrobenzene–naphthalene.*

Expt. No.	3	4	5	6
Biaryls (g.)	2·85	3·03	3·13	2·97
Residue (g.)	0·73	0·70	0·66	0·62
Nitrobiphenyls in biaryl fraction (%)	53·4	53·2	54·5	53·8
N-Nitrosoacetanilide accounted for in the biaryl fraction (%)	46·45	49·35	51·0	48·4

The mean nitrobiphenyl content of the biaryl fraction is thus 53·7% and hence, after allowance for the fact that a 4 : 1 molar mixture of nitrobenzene and naphthalene was used, ${}^{C_{10}H_8}_{Ph\cdot NO_2}K = 3{\cdot}36$.

DISCUSSION

It is clear that benzoyl peroxide is unsuitable for use in competitive phenylation experiments with mixtures of nitrobenzene and naphthalene, because whereas with naphthalene the predominant reaction is with the benzoyloxy-radical by substitution and hydrogen abstraction, the main reaction with nitrobenzene is with the phenyl radical by substitution. In addition it can be shown that in a competitive reaction with benzoyl peroxide more than 100% of the peroxide can be accounted for on the basis of the quantities of the free acid, the acid formed after hydrolysis and the biaryl fraction formed if this fraction is considered to consist solely of nitrobiphenyls and phenylnaphthalenes. It is likely that this anomaly is due, at least in part, to the formation of nitrophenylnaphthalenes resulting from the attack on nitrobenzene by naphthyl radicals produced by hydrogen-abstraction from naphthalene.

The identification of aniline after the hydrolysis stage in the working up of the product of the reaction of benzoyl peroxide with a mixture of nitrobenzene and naphthalene provides evidence of the fate of some of the hydrogen which is removed from the intermediate resulting from the attack on naphthalene by a free radical. The high reactivity of naphthalene towards free radicals results in an insufficiency of radicals (or benzoyl peroxide molecules) to dehydrogenate all the intermediate complexes and it is suggested that some of these are oxidised by nitrobenzene to give aniline which undergoes rapid reaction with benzoyl peroxide to give benzanilide. Nozaki and Bartlett[11] have drawn attention to the reactivity of aniline towards benzoyl peroxide, and other workers[12,13] have shown that benzanilide is in fact a major product of the reaction of benzoyl peroxide with aniline. These observations are in agreement with the fact that aniline is found only after the reaction product has been subjected to alkaline hydrolysis.

Partial Rate Factor for the Phenylation of Naphthalene.—The relative rate of the phenylation of naphthalene ${}^{C_{10}H_8}_{C_6H_6}K$ may be calculated from ${}^{C_{10}H_8}_{Ph\cdot NO_2}K$ and ${}^{Ph\cdot NO_2}_{C_6H_6}K$, the value for

[10] Hey, Moulden, and Williams, *J.*, 1960, 3769.
[11] Nozaki and Bartlett, *J. Amer. Chem. Soc.*, 1946, **68**, 1686.
[12] De Paolini, *Gazzetta*, 1930, **60**, 589.
[13] Horner and Schwenk, *Annalen*, 1950, **566**, 69.

which has been reported in Part XXIII [14] to be 2·94. Thus $^{C_{10}H_8}_{C_6H_6}K = {}^{C_{10}H_8}_{Ph\cdot NO_2}K \times {}^{Ph\cdot NO_2}_{C_6H_6}K = 3{\cdot}36 \times 2{\cdot}94 = 9{\cdot}9$. The value, $^{Ph\cdot NO_2}_{C_6H_6}K = 2{\cdot}94$, refers to a temperature of 80° but the variation with temperature is not considered to be serious. Huisgen and Grashey [5] have recorded a figure of 3·1 for $^{Ph\cdot NO_2}_{C_6H_6}K$ for a competitive phenylation reaction carried out at 25°. If F_1 and F_2 represent the partial rate factors for the phenylation of naphthalene at positions 1 and 2 respectively, then:

$$6\,{}^{C_{10}H_8}_{C_6H_6}K = 4F_1 + 4F_2$$

By using the isomer ratio 79·1 : 20·9 for the phenylation of naphthalene in positions 1 and 2 with *N*-nitrosoacetanilide at 25°, due to Huisgen and Grashey,[5] the following values are obtained for the partial rate factors: $F_1 = 11{\cdot}7$; $F_2 = 3{\cdot}1$. These results are considerably lower than those reported by Augood,[3] and Hey and Williams [2] for the benzoyl peroxide reaction now distrusted, but they are in reasonable agreement with the more recent results reported by Huisgen, Jakob, and Grashey [6] who used an entirely different experimental technique.

Some values derived from theoretical calculations for the total and partial rate factors for the phenylation of naphthalene are given in Table 3. The calculations based on free

TABLE 3. *Calculated total and partial rate factors for the phenylation of naphthalene.*[a]

Method	F_1	F_2	$^{C_{10}H_8}_{C_6H_6}K$
Free valence numbers	11·29	1·10	8·26
,, ,,	13·71	1·34	10·03
Atom localisation energies	$87{\cdot}79 \times 10^3$	19·71	$4{\cdot}39 \times 10^4$

[a] See Augood and Williams, *Chem. Rev.*, 1957, **57**, 123.

valence numbers agree well with experiment but those based on atom localisation energies are far too large. Williams [15] has suggested that this gross overestimate may be due to the inappropriate use of the carbon–carbon resonance integral (β) in the calculation of the localisation energies. For instance, Dewar, Mole, and Warford [16] have shown that, for substitution of polycyclic hydrocarbons with reagents of high intrinsic reactivity, such as methyl radicals, agreement between experimentally determined and calculated relative rates of reactions is obtained only when parameters β'_x which have much lower numerical values than β, are used in the calculations. This arises from the circumstance that the σ-complexes which were originally considered by Wheland [17] to approximate closely to the transition states for reaction at the various sites are, in fact, true intermediates representing minima in the potential energy curves, and that the actual transition states are closer to the parent aromatic system than to the Wheland structures. The hybridisation of the carbon atom *r* at which substitution occurs is therefore intermediate between sp^2 and sp^3, and not sp^3 as in the Wheland structure. Some allowance must, therefore, be made for the incomplete removal of carbon atom *r* from the system over which delocalisation occurs, and β should be replaced, for substitution by the reagent X, by β'_x, which is given by $\beta'_x = \beta - \beta_x$, where β_x is the value of the resonance integral between atom *r* and the adjacent carbon atoms in the transition state for substitution by X. Since the intrinsic reactivity of the phenyl radical is probably comparable with that of the methyl radical, these considerations probably also apply to phenylation, and if this is so the discrepancy between the experimental and calculated reactivities is readily understood.

The partial and total rate factors for the phenylation of naphthalene are the largest yet reported for an aromatic compound, but the increased reactivity of naphthalene relative to benzene is very much smaller for phenylation than for nitration. The partial rate factors for the nitration of naphthalene are $F_1 = 470$ and $F_2 = 50$,[16] which indicates

[14] Hey, Orman, and Williams, *J.*, 1961, 565.
[15] Williams, "Homolytic Aromatic Substitution," Pergamon Press Ltd., London, 1960, p. 22.
[16] Dewar, Mole, and Warford, *J.*, 1956, 3581.
[17] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900.

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that the phenyl radical is much less sensitive than the nitronium ion towards increased electron availability at the site of substitution. The decreased importance of electronic effects in radical substitution is also emphasised by the fact that $F_1/F_2 = 9{\cdot}4$ for nitration but only 3·8 for phenylation. Smid and Szwarc [18] recently determined the relative methyl, ethyl, and propyl affinities of naphthalene relative to benzene and found them to be 30, 34·5, and 34·2 respectively.

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King's College (University of London), Strand, London, W.C.2.
Birkbeck College (University of London), Malet Street, London, W.C.1.
The University, Leeds, 2. [*Received, December 16th*, 1960.]

[18] Smid and Szwarc, *J. Amer. Chem. Soc.*, 1957, **79**, 1534.

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598. *Homolytic Aromatic Substitution. Part XXVI.* The Reactions of Some Aroyl Peroxides with Naphthalene.*

By D. I. Davies, D. H. Hey, and Gareth H. Williams.

The products of reactions of *o*- and *p*-nitrobenzoyl, *o*- and *p*-chlorobenzoyl, and 1- and 2-naphthoyl peroxide with naphthalene have been subjected to quantitative study. The composition of the mixtures of isomeric naphthols arising from the hydrolysis of the naphthyl esters formed in these reactions, and of the mixtures of isomeric binaphthyls formed in the reactions with 1- and 2-naphthoyl peroxide, have been determined by infrared spectroscopy. The results are discussed in terms of the polar characteristics of the various radicals, and are shown to be consistent with current theory.

The results reported in Part XIII [1] indicate that the free radicals formed by the decomposition of benzoyl peroxide react with naphthalene in three distinct ways. These are: (*a*) substitution by benzoyloxy-radicals to give 1- and 2-naphthyl benzoate, (*b*) substitution by phenyl radicals to give 1- and 2-phenylnaphthalene, and (*c*) hydrogen abstraction by benzoyloxy-radicals to give 1- and 2-naphthyl radicals, which then react with naphthalene by substitution to give 1,1′- 1,2′-, and 2,2′-binaphthyl. The distribution of the various isomers of the different products was also measured. It was therefore considered of interest to investigate the reactions of some other aroyl peroxides with naphthalene, in order to determine the influence of substituents in the nuclei of the aryl and aroyloxy-radicals on the relative extent to which processes (*a*), (*b*), and (*c*) occur, and on the isomer distribution in the various products. In addition, in order to throw more light on the mechanism of process (*c*), the reactions of 1- and 2-naphthoyl peroxide with naphthalene were studied. The results of these experiments, in which *o*- and *p*-chlorobenzoyl, *o*- and *p*-nitrobenzoyl, and 1- and 2-naphthoyl peroxide were allowed to decompose in naphthalene, are now reported and discussed.

Experimental

Naphthalene was purified as described in Part XIII.[1] The aroyl peroxides were prepared from the corresponding acid chlorides by Hey and Walker's standard method.[2] The m. p.s of the products were all in agreement with those reported by Hey and Walker,[2] with the exception of *o*-chlorobenzoyl peroxide, which was not prepared by those workers. Our results for this compound are, however, in agreement with those of Breitenbach and Bremer [3] who reported its preparation.

* Part XXV, preceding paper.

[1] Davies, Hey, and Williams, *J.*, 1958, 1878.
[2] Hey and Walker, *J.*, 1948, 2213.
[3] Breitenbach and Bremer, *Ber.*, 1943, **76**, 1124.

The isomeric binaphthyls were prepared as described in Part XIII.[1]

1-*Naphthyl* p-*chlorobenzoate* was prepared by reaction of 1-naphthol (4 g.) with *p*-chlorobenzoyl chloride (5 g.) in the presence of pyridine (10 ml.). The mixture was left overnight, diluted with water, and filtered. The ester (6·5 g.) after crystallisation from methanol had m. p. 115·5° (Found: C, 72·1; H, 3·9; Cl, 12·4. $C_{17}H_{11}ClO_2$ requires C, 72·2; H, 3·9; Cl, 12·5%).

The other esters were prepared by analogous methods.

2-*Naphthyl* p-*chlorobenzoate*, after crystallisation from methanol, had m. p. 121·5° (Found: C, 71·6; H, 3·6; Cl, 12·9%). 1-*Naphthyl* o-*chlorobenzoate* had m. p. 53° (from methanol) (Found: C, 72·7; H, 3·7; Cl, 13·0%). 2-*Naphthyl* o-*chlorobenzoate* had m. p. 88·5° (from ethanol) (Found: C, 72·5; H, 4·0; Cl, 12·2%). 1- and 2-Naphthyl *p*-nitrobenzoate had m. p.s 143° and 169° respectively (lit.,[4] 143° and 169° respectively). 1-*Naphthyl* o-*nitrobenzoate* had m. p. 101° (from ethanol) (Found: C, 70·0; H, 4·0; N, 5·0. $C_{17}H_{11}NO_4$ requires C, 69·6; H, 3·8; N, 4·8%). 2-Naphthyl *o*-nitrobenzoate had m. p. 113·5° (lit.,[5] 112°) (Found: C, 69·7; H, 3·5; N, 4·6%).

Decomposition of Aroyl Peroxides in Naphthalene.—The aroyl peroxide was allowed to decompose in molten naphthalene (100 g.) in a thermostat at 85° for 72 hr. The initial concentration of the peroxide was 0·02M. The products were worked up as described in Part XIII [1] for the reaction of benzoyl peroxide with naphthalene. The free aroic acid, and the acid formed by the hydrolysis of esters were generally obtained in a pure state, and had m. p.s very close to those recorded in the literature.

Reaction of p-*Nitrobenzoyl Peroxide with Naphthalene.*—In experiment 1 the esters were hydrolysed as described in Part XIII,[1] but only a trace of phenolic material was obtained from the hydrolysate together with a dark red viscous gum, from which no crystalline product could be isolated, in place of the expected *p*-nitrobenzoic acid. The same result was obtained when an authentic mixture of 1- and 2-naphthyl *p*-nitrobenzoate was hydrolysed under the same conditions. Similar results were also obtained when more dilute (2N) sodium hydroxide solution was used for the hydrolysis. The biaryl fraction obtained from this experiment contained no nitrogen, and its infrared spectrum showed it to be mixture of the isomeric binaphthyls. Fractional crystallisation of a portion of this mixture from light petroleum (b. p. 80—100°) gave white crystals the analysis of which was consistent with that required for binaphthyl (Found: C, 94·2; H, 5·5. Calc. for $C_{20}H_{14}$: C, 94·45; H, 5·55%).

In experiment 2, the hydrolysis stage was omitted, and the esters and biaryls were distilled together. The infrared spectrum of this fraction revealed the presence of 1- and 2-naphthyl *p*-nitrobenzoate. Specimens of both these esters were obtained by fractional crystallisation from methanol, and their m. p.s were in agreement with those reported in the literature and not depressed on admixture with authentic specimens. The results of these experiments are summarised in Table 2.

Reaction of o-*Nitrobenzoyl Peroxide with Naphthalene.*—In experiment 3 the esters were hydrolysed by refluxing the mixture for 24 hr. with two successive portions (100 ml.) of 2N-sodium hydroxide since a preliminary experiment showed that hydrolysis with 5N-sodium hydroxide, as described in Part XIII,[1] led to intractable, resinous products. Hydrolysis with 2N-alkali gave *o*-nitrobenzoic acid and a mixture of 1- and 2-naphthol. The biaryl fraction obtained from this experiment contained no nitrogen, and its infrared spectrum showed it to be a mixture of the isomeric binaphthyls. Fractional crystallisation of a portion of this mixture from light petroleum (b. p. 80—100°) gave white crystals (m. p. 130—135°) whose infrared spectrum showed it to be 1,1′-binaphthyl contaminated with a trace of the 1,2′-isomer (Found: C, 93·9; H, 5·6%).

No hydrolysis was carried out on the product of experiment 4, the esters and biaryls being distilled together. The infrared spectrum of this distillate revealed the presence of both 1- and 2-naphthyl *o*-nitrobenzoate, and fractional crystallisation from methanol gave a pure specimen of 1-naphthyl *o*-nitrobenzoate (m. p. and mixed m. p. 101°) (Found: C, 70·2; H, 3·7; N, 5·1%). The infrared spectrum of this compound was identical with that of an authentic specimen. The results of these experiments are summarised in Table 2.

Reaction of p-*Chlorobenzoyl Peroxide with Naphthalene.*—The product of experiment 5 was worked up as described in Part XIII,[1] and a mixture of 1- and 2-naphthol and *p*-chlorobenzoic

[4] Vogel, "A Text-Book of Practical Organic Chemistry," Longmans, Green and Co. Ltd., London, 1948.

[5] Barnett and Nixon, *Chem. News*, 1924, **129**, 190.

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acid was obtained by the hydrolysis of the esters. Slow crystallisation of the biaryl fraction (1·39 g.) from light petroleum (b. p. 80—100°) gave 2,2′-binaphthyl (0·041 g.; m. p. and mixed m. p. 186°). Analysis of the residue obtained on evaporation of the mother-liquors gave: C, 89·55; H, 5·35; Cl, 4·7%; and the infrared spectrum showed it to contain both 1,1′- and 1,2′-binaphthyl, together with some other material. If this residue is assumed to be a mixture of *p*-chlorophenylnaphthalenes and binaphthyls, the above analysis indicates that the chloro-compounds are present in the biaryl fraction to the extent of 30·4% (0·42 g.). It was not possible to separate quantitatively the *p*-chlorophenylnaphthalenes from the binaphthyls by distillation or by chromatography on alumina. However, fractional crystallisation from light petroleum (b. p. 80—100°) gave white crystals, m. p. 135°, whose analysis is consistent with their being a mixture of 1,1′- and 1,2′-binaphthyl (Found: C, 94·4; H, 5·5%).

No hydrolysis was carried out on the product of experiment 6, the esters and biaryls being distilled together. Fractional crystallisation of this mixture from methanol, followed by recrystallisation of the crude products to constant m. p. gave the following: (i) 2,2′-binaphthyl, m. p. and mixed m. p. 186° (Found: C, 94·35; H, 5·4%); (ii) 1,1′-binaphthyl, m. p. and mixed m. p. 160° (Found: C, 94·9; H, 5·8%); (iii) 1-naphthyl *p*-chlorobenzoate, m. p. and mixed m. p. 115·5° (Found: C, 72·3; H, 3·9; Cl, 12·8%). The infrared spectra of these compounds were identical with those of authentic specimens. No pure specimen of 2-naphthyl *p*-chloro-benzoate could be isolated, although its presence was indicated by the infrared spectra of the residues obtained by working up the mother-liquors remaining after the isolation of the above compounds. The results of these experiments are summarised in Table 2.

Reaction of o-*Chlorobenzoyl Peroxide with Naphthalene.*—The products of experiments 7 and 8 were worked up as described in Part XIII,[1] and biaryl fractions were collected which consisted of binaphthyls and *o*-chlorophenylnaphthalenes. These fractions were analysed for chlorine and their composition calculated from the analyses. These results are given in Table 1.

Crystallisation of a portion of the biaryl fraction from experiment 7 from light petroleum (b. p. 80—100°) gave a small amount of 2,2′-binaphthyl (0·005 g.) (m. p. and mixed m. p. 182°; correct infrared spectrum). Specimens of *o*-chlorobenzoic acid and mixtures of 1- and 2-naphthol were obtained from the ester hydrolysates. The results of these experiments are summarised in Table 2.

TABLE 1. *Analysis of biaryl fractions in Expts.* 7 *and* 8.

Expt.	Wt. of biaryl fraction (g.)	Cl (%)	*o*-Chlorophenylnaphthalenes (%)
7	1·50	6·95	47
8	1·48	5·7	39

TABLE 2. *Products of reactions of aroyl peroxides with naphthalene.*

Experiment No.:	1	2	3	4	5	6	7	8
Substituent in phenyl group of peroxide	*p*-NO_2	*p*-NO_2	*o*-NO_2	*o*-NO_2	*p*-Cl	*p*-Cl	*o*-Cl	*o*-Cl
Peroxide used (g.)	5·182	5·182	5·182	5·182	4·854	4·854	4·854	4·854
Free acid (g.)	2·91	2·88	2·76	2·76	3·15	3·14	2·70	2·71
Acid formed by hydrolysis of esters (g.)	0·98		2·28		1·49		1·66	1·65
Naphthols (g.)	0·19		1·43		0·94		0·80	0·86
Binaphthyls (g.)	0·46		0·24		0·97		0·80	0·91
Arylnaphthalenes (g.)	0·0		0·0		0·42		0·70	0·57
Esters and biaryls (g.)		4·10		4·16		3·97		
Esters (g.) *		3·64		3·92		2·58		
Non-volatile residue (g.)	0·02	0·18	0·02	0·19	0·02	0·18	0·13	0·10
Peroxide accounted for (%)		95·05	96·66	95·75	100·7	99·19	98·7	96·99

* These quantities were calculated by subtraction of the combined yields of binaphthyls and aryl-naphthalenes obtained in experiments 1, 3, and 5 from the combined yields of esters and biaryls obtained from experiments 2, 4, and 6 respectively.

In a further experiment the hydrolysis stage was omitted, and the esters and biaryls were distilled together. Fractional crystallisation of this distillate from methanol gave 1,1′-bi-naphthyl (m. p. and mixed m. p. 160°) (Found: C, 94·2; H, 5·4%). No other pure compounds could be obtained from this mixture.

Reaction of 1-*Naphthoyl Peroxide with Naphthalene.*—Experiments 9 and 10 were conducted as described in Part XIII.[1] When the peroxide was added to the molten naphthalene, an immediate, vigorous evolution of gas (probably carbon dioxide) was observed. This may be connected with the comparatively low percentage of the peroxide which could be accounted for in these reactions. The first distillation of the biaryl fractions gave products which were contaminated with 1-naphthoic acid and unhydrolysed esters. These compounds were removed by boiling the biaryl fractions under reflux for 24 hr. with further portions of 5N-sodium hydroxide. Although repeated attempts were made, no 2,2′-binaphthyl could be isolated from these fractions, and it is therefore concluded that little if any of this isomer was present. A small liquid fraction, b. p. 66°/0·1 mm., was also obtained in the distillation of these "biaryl fractions." This material was not identified, but its analysis indicates that it was not a hydrocarbon (Found: C, 83·9; H, 7·1%).

The products obtained in these experiments are summarised in Table 3.

Reaction of 2-*Naphthoyl Peroxide with Naphthalene.*—Experiment 11 was conducted as described in Part XIII.[1] During the hydrolysis of the esters a large quantity of a solid was precipitated, which was subsequently shown to be sodium 2-naphthoate (2-naphthoic acid liberated, m. p. and mixed m. p. 182—185°). Moreover, the biaryl fraction obtained by distillation of the neutral residue after the hydrolysis of esters was found to be contaminated with unhydrolysed esters and 2-naphthoic acid. Consequently, in experiments 12 and 13, the residues after removal of naphthalene and free 2-naphthoic acid were refluxed with two successive portions of sodium hydroxide solution to ensure complete hydrolysis, and water (250 ml.) was added when hydrolysis was complete in order to take up the precipitated sodium 2-naphthoate. The results obtained in these experiments are given in Table 3, and those of experiments 12 and 13 are considered to be the more reliable.

TABLE 3. *Products of reactions of* 1- *and* 2-*naphthoyl peroxides* (5·34 g.) *with naphthalene* (100 g.).

Experiment No.:	9	10	11	12	13
Naphthoyl peroxide	1-	1-	2-	2-	2-
Free acid (g.)	1·92	1·96	2·90	2·88	2·87
Acid formed by hydrolysis of esters (g.)	1·60	1·62	0·43	1·95	2·00
Naphthols (g.)	1·04	0·97	0·47	0·93	0·99
Liquid, b. p. 66°/0·1 mm. (g.)	0·06	0·05			
Binaphthyls (g.)	1·17	1·17	1·20	1·21	1·19
Non-volatile residue (g.)	0·12	0·19	0·14	0·18	0·17
Peroxide accounted for (%)	80·3 *	81·3 *	—	89·9 †	90·7 †

* Since no 2,2′-binaphthyl was isolated in this reaction, it is assumed for the purpose of this calculation that the binaphthyls were formed entirely by direct substitution of 1-naphthyl radicals, derived from the peroxide, in naphthalene; and hence the binaphthyls are taken into account in deriving these figures.

† These figures were arrived at without reference to the binaphthyls, since, because all three isomeric binaphthyls are formed, not all of them could have been formed by direct substitution of 2-naphthyl radicals in naphthalene. It is, therefore, impossible to obtain an accurate estimate of the amount of binaphthyls formed by direct substitution.

TABLE 4. *Ratio of isomeric naphthols and binaphthyls formed in experiments* 1—13.

		Naphthols (%)		2,2′-Binaphthyl	Total Binaphthyls (%)		
Expt. No.	Peroxide	1-	2-	(g.)	1,1′-	1,2′-	2,2′-
1	*p*-Nitrobenzoyl	72·3	27·7				
3	*o*-Nitrobenzoyl	81·0	19·0				
5	*p*-Chlorobenzoyl	75·4	24·6				
7	*o*-Chlorobenzoyl	70·8	29·2				
8	*o*-Chlorobenzoyl	75·2	24·8				
9	1-Naphthoyl	82·1	17·9	0·0	69·0	31·0	0·0
10	1-Naphthoyl	82·2	17·8	0·0	69·6	30·4	0·0
12	2-Naphthoyl	68·6	31·4	0·098	36·7	55·2	8·1
13	2-Naphthoyl	66·9	33·1	0·107	34·8	56·3	8·9

The infrared spectra of the biaryl fractions were consistent with their being mixtures of the three isomeric binaphthyls. Pure specimens of 1,1′- and 2,2′-binaphthyl were isolated from them.

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Determination of Ratios of Isomers.—The spectrographic analysis of the mixtures of binaphthyls and naphthols from experiments 1—13 was conducted by the method described in Part XIII.[1] The results are given in Table 4. The results of tests of the accuracy of the methods of analysis of mixtures of binaphthyls and naphthols (by the analysis of synthetic mixtures of known composition) were also described in Part XIII.[1]

Discussion

The molar yields of the various products of the reactions of the aroyl peroxides with naphthalene are summarised in Table 5.

Since both the free acid and the acid formed by the hydrolysis of esters were invariably obtained in a reasonably pure state, very little further substitution of these acids or esters could have occurred. This supports the contention [1] that naphthalene is a " fast " solvent towards homolytic attack. This view is also supported by the small amounts of involatile residue formed in these reactions.[6]

The most striking feature of these results is the decrease in the yield of esters, and the concomitant increase in the yield of arylnaphthalenes along the series nitrobenzoyl peroxides, chlorobenzoyl peroxides, benzoyl peroxide. These phenomena appear to be linked with the electrophilic character of the corresponding aroyloxy-radicals, which might be expected to decrease in the order, *o*- and *p*-$NO_2 \cdot C_6H_4 \cdot CO \cdot O\cdot$ > *o*- and *p*-$Cl \cdot C_6H_4 \cdot CO \cdot O\cdot$ > $C_6H_5 \cdot CO \cdot O\cdot$. Since naphthalene is very reactive towards electrophilic reagents reaction of the aroyloxy-radicals with naphthalene tends to supersede the competing reaction of decarboxylation as the electrophilic character is increased. The effect of nuclear substituents on the ease of decarboxylation is difficult to predict as neither the aroyloxy- nor the aryl radical can be appreciably stabilised by nuclear substituents. The only additional canonical forms which can be written for these radicals necessarily contain an additional dipole, and hence can make only very small contributions. Any such effects are therefore likely to be small, and consequently the effect of substituents on the reactivity of aroyloxy-radicals in nuclear substitution is, as discussed above, likely to be the dominating influence on their fate.

The position of the naphthoyl peroxides in this series (cf. Table 5) indicates that 1- and 2-naphthoyloxy-radicals are not very different from benzoyloxy-radicals with regard either to polarity or to stability.

Although the formation of binaphthyls in these reactions is due, in the first instance, to attack on the nucleus of naphthalene by aroyloxy-radicals (cf. Part XIII [1]), the yield of binaphthyls (Table 5) varies with the nature of the aroyl peroxide in the opposite sense to that of the esters formed as a result of substitution by aroyloxy-radicals. This is reasonable since the binaphthyls arise by attack of aroyloxy-radicals on hydrogen attached

Table 5. *Yields, in moles/mole of peroxide, of the products of aroyl peroxide–naphthalene reactions.*

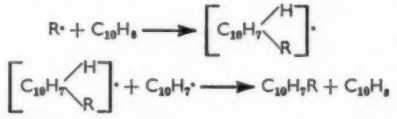
Peroxide	Free acid	Esters	Arylnaphthalenes	Binaphthyls
Benzoyl [1]	1·12	0·55	0·20	0·29
p-Nitrobenzoyl	1·11	0·80	0·0	0·12
o-Nitrobenzoyl	1·06	0·87	0·0	0·06
p-Chlorobenzoyl	1·29	0·61	0·11	0·24
o-Chlorobenzoyl	1·11	0·68	0·17	0·21
1-Naphthoyl	0·72	0·60	0·29	
2-Naphthoyl	1·07	0·72	0·30	

to nuclear carbon, giving the appropriate aroic acid together with 1- and 2-naphthyl radicals which then effect substitution in the 1- and the 2-position of other naphthalene molecules. The esters, on the other hand, are formed by attack of the aroyloxy-radicals on the nuclear carbon atoms. Whereas the latter process would be expected to become

[6] Williams, " Homolytic Aromatic Substitution," Pergamon Press Ltd., London, 1960, pp. 59, 65.

more favoured as the electrophilic character of the attacking radical is increased, the results indicate that the former has the opposite polar requirement since the two reactions are direct competitors. Hambling, Hey, Pengilly, and Williams [7] have shown that the analogous reaction of hydrogen-abstraction from the side-chain of toluene by *para*-substituted aryl radicals is favoured by increasing nucleophilic character on the part of the radicals, and similar considerations might be expected to apply in the present reactions.

The amounts of the products obtained in reactions with 1-naphthoyl peroxide, especially with regard to the free 1-naphthoic acid formed, seem to be out of harmony with the other members of the series. Also (cf. Experimental Section), the amount of this peroxide accounted for as identified products was unusually low. These anomalies are probably connected with the vigorous evolution of much carbon dioxide which occurs in this reaction. 1-Naphthyl radicals must therefore be formed rapidly and in high yield. These entities have a certain amount of resonance stabilisation and consequently may be present in sufficient concentration to contribute to the dehydrogenation of the intermediate σ-complexes of substitution reactions, thereby giving rise to the formation of naphthalene:



where R = $C_{10}H_7$ or $C_{10}H_7$·CO·O.

It is, of course, impossible to distinguish naphthalene formed in this way from solvent naphthalene, except by the use of isotopically labelled reagents, and the observable results of such a process should be (*a*) a decrease in the yield of 1-naphthoic acid, and (*b*) a decrease in the amount of the peroxide accounted for. These are, in fact, the observed phenomena.

The ratios of the isomeric naphthols arising from hydrolysis of the esters formed on the decomposition of aroyl and naphthoyl peroxides in naphthalene are given in Table 4. These may be compared with the corresponding ratio for the decomposition of benzoyl peroxide in naphthalene [1] (1-naphthol, 72·9%; 2-naphthol, 27·1%). The results obtained with *p*-nitrobenzoyl peroxide are unreliable, since the hydrolysis of the esters obtained from its reaction with naphthalene gave only a very low yield of naphthols together with a red gum in place of the expected *p*-nitrobenzoic acid; these figures are, therefore, disregarded in the following discussion. The results indicate that the presence of nitro- (and to a smaller extent chloro-) substituents in the attacking aroyloxy-radicals increases the amount of substitution which occurs at the 1-position of naphthalene. This is consistent with the increased electrophilic character of these radicals, since naphthalene is substituted predominantly in the 1-position by electrophilic reagents.[8] This interpretation is in accord with the results obtained by Marshall and Waters [9] on the reaction of naphthalene with aryl radicals containing substituents of various polar characteristics. It was found that electron-withdrawing substituents in the aryl radicals increased, and electron-repelling substituents decreased, the proportion of 1-substitution.

On the basis of the above argument, and in view of the results given in Table 4, it might be inferred that the 1-naphthoyloxy-radical is more, and the 2-naphthoyloxy-radical less, electrophilic than the benzoyloxy-radical. However, an alternative interpretation, which is peculiarly applicable to these reactions, namely, that some 1- and 2-naphthyl naphthoate may be formed by the intramolecular loss of carbon dioxide from 1- and 2-naphthoyl peroxide, respectively, cannot be ruled out at present.

The mean ratios in which the isomeric binaphthyls are formed from the reactions of 1- and 2-naphthoyl and benzoyl [1] peroxide with naphthalene are given in Table 6. The

[7] Hambling, Hey, Pengilly, and Williams, unpublished observations.
[8] Cf. Dewar and Mole, *J.*, 1956, 1441.
[9] Marshall and Waters, *J.*, 1959, 381.

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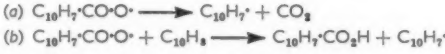
wide differences revealed are expected, since, in the reactions with the naphthoyl peroxides, binaphthyls can be formed in two ways, according as the naphthyl radicals are derived by

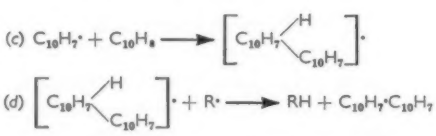
TABLE 6. *Formation of isomeric binaphthyls in reactions with naphthalene.*

Peroxide	1,1′-Binaphthyl (%)	1,2′-Binaphthyl (%)	2,2′-Binaphthyl (%)
1-Naphthoyl	69	31	0
2-Naphthoyl	36	56	8
Benzoyl	54	42	4

decarboxylation of naphthoyloxy-radicals (*a*) or by hydrogen-abstraction from solvent naphthalene (*b*):



The naphthyl radicals formed by either of these processes may then effect nuclear substitution in naphthalene [reactions (*c*) and (*d*)]:



where R· is any radical present in solution which is capable of oxidising the intermediate σ-complex. If all the naphthyl radicals were formed by reaction (*b*), then it can be predicted that the ratio of the isomeric binaphthyls formed should be similar to that formed in the reaction of benzoyl peroxide with naphthalene, in which this is the only source of naphthyl radicals, provided that the assumption is made that benzoyloxy- and naphthoyloxy-radicals behave similarly in the hydrogen-abstraction reaction (*b*). Since the course of this reaction is largely determined by polar influences (see above), and since there is no *a priori* reason to suppose that the polar characteristics of benzoyloxy- and naphthoyloxy-radicals differ widely, this assumption is accepted as reasonable. The extent of the divergence from the isomer ratio obtained with benzoyl peroxide can therefore be regarded as a measure of the incidence of the direct naphthylation [(*a*) followed by (*c*) and (*d*)]. In the reaction with 2-naphthoyl peroxide, 1,1′-binaphthyl can arise only as a result of the abstraction reaction [(*b*) followed by (*c*) and (*d*)]. If it is now assumed that 1,2′- and 2,2′-binaphthyl are also formed by this reaction in the same ratio to 1,1′-binaphthyl as in the corresponding reaction with benzoyl peroxide, the following isomer ratio for binaphthyls formed in this way can be obtained: 1,1′- 35·7; 1,2′- 27·7; 2,2′- 2·6%. The sum of these figures, 66%, represents the proportion of the total yield of binaphthyls which is formed by the abstraction process. It then follows that the remainder of the binaphthyl (34%) represents the binaphthyls formed by direct substitution, and in the ratio obtained by subtraction, namely, 1,2′- 28·1; 2,2′- 5·9%. Thus the direct 2-naphthylation of naphthalene gives 1,2′- and 2,2′-binaphthyl in the following ratio: 1,2′- 82·6; 2,2′- 17·5%. These figures are very similar to those obtained for the ratio of isomeric phenylnaphthalenes (the corresponding products of direct substitution) obtained in the reaction of benzoyl peroxide with naphthalene (1-, 82; 2-, 18%),[1] thus confirming the postulated similarity in polar characteristics of the radicals derived from benzoyl and naphthoyl peroxides.

No calculation of this type can, however, be performed on the results obtained for the reaction of 1-naphthoyl peroxide with naphthalene, since no 2,2′-binaphthyl could be isolated from the products of this reaction. The complete absence of this product is hardly to be expected, since this would mean that no hydrogen-abstraction took place. The amount of 2,2′-binaphthyl would, however, be expected to be very small since the

2-position is much the less reactive in two successive reactions, and it may well be that this small amount escaped detection by the experimental techniques employed.

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KING'S COLLEGE, STRAND, LONDON, W.C.2.
BIRKBECK COLLEGE, MALET STREET, LONDON, W.C.1.
THE UNIVERSITY, LEEDS, 2.

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599. *Sulphitobis(ethylenediamine)cobalt*(III) *Complexes.*

By M. E. BALDWIN.

The following complexes have been prepared: *cis*-[Co $en_2(SO_3)_2$]Na; *trans*-[Co $en_2(SO_3)_2$]Na; [Co en_2SO_3,Cl]^0; [Co en_2SO_3,OH]^0; [Co en_2SO_3,NH_3]Cl; [Co en_2SO_3,OH_2]ClO_4; in these the sulphito-group is unidentate; complexes [Co en_2SO_3]X, where X = ClO_4, NO_2, I, or SCN, have also been prepared where the sulphito-group probably occupies two co-ordinate positions. Infrared and visible absorption spectra of the compounds have been measured.

Disulphito-complexes.—Although Riesenfeld [1] in 1923 and Klement [2] in 1926 had obtained compounds [Co $en_2(SO_3)_2$]Na, the configurations of these had not been determined. Two isomeric forms of the sodium disulphitobis(ethylenediamine)cobaltate(III) salt have been obtained in the present work, and the configurations have been assigned on the basis of visible and infrared spectral data.

The *cis*-isomer was obtained by reaction of an excess of sodium sulphite with *cis*- or *trans*-[Co en_2Cl_2]Cl. The infrared absorption spectrum of this compound showed two peaks in the CH_2 rocking region [3] and a band structure generally more complex than that of its isomer.

The *trans*-isomer was obtained from *trans*-[Co en_2NCS,OH_2]Br_2 by the action of an excess of sodium sulphite. This compound showed one sharp band in the CH_2 rocking region.

The visible absorption spectra supported these assignments.[4] The absorption maximum of the *cis*-isomer was at a lower wavelength and had a larger extinction coefficient ($\varepsilon_{max.}$ 406 at 431 mμ) than the *trans*-isomer ($\varepsilon_{max.}$ 313 at 440 mμ).

Monosulphito-complexes containing the Unidentate Sulphito-group.—The reaction of dilute aqueous sodium sulphite in the cold with *cis*- or *trans*-[Co en_2Cl_2]Cl produced a pink-brown compound of the empirical formula Co en_2SO_3,Cl,H_2O (I). The reactions of this product corresponded to a large extent to those described by Werner [5] for the compound formulated as [Co en_2SO_3]Cl,H_2O. Further examination showed that Werner's structure could not be correct. The general reactions may be correlated if it is assumed that the solid is [Co en_2SO_3,Cl]^0,H_2O which dissolves in water to give a solution of the salt [Co en_2SO_3,OH_2]Cl (II). The evidence may be summarised as follows:

(*a*) The solid (I) was dehydrated at 120°. The infrared spectrum of the anhydrous compound was little different from that of the original.

(*b*) The solid (I) dissolved in water to give a brown conducting solution (0·00169M), which had a molar conductivity of 111·3 ohm^{-1}, indicating that a 1 : 1 electrolyte was present.

(*c*) Chloride ions were precipitated quantitatively from the aqueous solution on the

[1] Riesenfeld, *Z. anorg. Chem.*, 1923, **132**, 99.
[2] Klement, *Z. anorg. Chem.*, 1926, **150**, 117.
[3] (*a*) Morris and Busch, *J. Amer. Chem. Soc.*, 1960, **82**, 1521; (*b*) Baldwin, *J.*, 1960, 4361.
[4] Basolo, *J. Amer. Chem. Soc.*, 1950, **72**, 4393; Basolo, Ballhausen, and Bjerrum, *Acta Chem. Scand.*, 1955, **9**, 810.
[5] Werner, *Annalen*, 1912, **386**, 83.

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addition of silver nitrate, without change in the visible absorption spectrum, *i.e.*, the complex species in solution was unaffected.

(*d*) The aqueous solution contained one equivalent of titratable hydrogen ion, which is consistent with the presence of an acidic aquo-group:

$$[Co\ en_2SO_3,OH_2]^+ + OH^- = [Co\ en_2SO_3,OH]^0 + H_2O$$

The hydroxosulphitobis(ethylenediamine)cobalt(III) compound has been isolated and is a non-electrolyte.

(*e*) The existence of the aquosulphitobis(ethylenediamine)cobalt(III) cation was confirmed by isolation of a yellow-brown, crystalline perchlorate that could not be dehydrated without change in character (solubility and colour; cf. p. 3127). The visible absorption spectrum of the perchlorate, $[CO\ en_2SO_3,OH_2]ClO_4$, was identical with that of the original compound (I) in solution.

(*f*) Concentrated hydrochloric acid converted the perchlorate into a pink solid whose infrared spectrum and analysis were identical with those of the original compound.

Addition of sodium thiocyanate to a solution of the chloro-compound (I) produced pale brown needles, $Co\ en_2SO_3,NCS,2H_2O$. The infrared spectrum of this solid showed conclusively the presence of co-ordinated thiocyanate,[6] so the compound may be formulated $[Co\ en_2SO_2,NCS]2H_2O$. Its aqueous solution ($8{\cdot}6 \times 10^{-4}$M) had a molar conductivity of 33·5 ohm^{-1}, indicating rapid establishment of the aquation equilibrium:

$$[Co\ en_2SO_3,NCS]^0 + H_2O \rightleftharpoons [Co\ en_2SO_3,OH_2]^+ + SCN^-$$

In contrast to the aquation of the chlorosulphito-compound this reaction did not go to completion. The equilibrium was, however, displaced to the right by the addition of silver nitrate: silver thiocyanate was precipitated and the spectrum of the remaining solution was identical with that of $[Co\ en_2SO_3,OH_2]^+$ but different from that of the aquation equilibrium solution.

The compound $[Co\ en_2SO_3,OH]^0$, which was prepared by the reaction of hydroxide ion on $[Co\ en_2SO_3,Cl]^0$, behaved as a non-electrolyte in methanol solution, but an aqueous 0·002M-solution had a molar conductivity of 24 ohm^{-1}.

The salt $[Co\ en_2SO_3,NH_3]Cl$ was prepared by the action of dilute ammonia solution on the original compound (I). It behaved as a 1 : 1 electrolyte in water.

The maxima and minima of the visible and ultraviolet absorption spectra of various aqueous solutions are shown in Table 1. Beer's law was not obeyed in the ultraviolet

TABLE 1. *Wavelength* (mμ) *and molar extinction coefficients of absorption bands of unidentate sulphito-compounds in the region* 600—200 mμ.

Concn. (mmole $l.^{-1}$)	$\lambda_{max.}$	log $\varepsilon_{max.}$	$\lambda_{min.}$	log $\varepsilon_{min.}$	Concn. (mmole $l.^{-1}$)	$\lambda_{max.}$	log $\varepsilon_{max.}$	$\lambda_{min.}$	log $\varepsilon_{min.}$
$[Co\ en_2SO_3,NH_3]Cl$					$[Co\ en_2SO_3,NCS]$				
1·420	463	2·210	395	1·505	0·460	452	2·335	391	1·702
0·116	272	4·150	244	3·499	0·112	275	4·219	242	3·587
0·046	272	4·130	244	3·491					
					$[Co\ en_2SO_3,OH]$				
					0·715	460	2·380	401	1·764
					0·143	275	3·852	245	3·176

region. It appeared that ion-pairing occurred. In the case of the " non-ionic " compounds the products of aquation might aggregate to form a species of the type $[Co\ en_2SO_3,OH_2]^+NCS^-$.

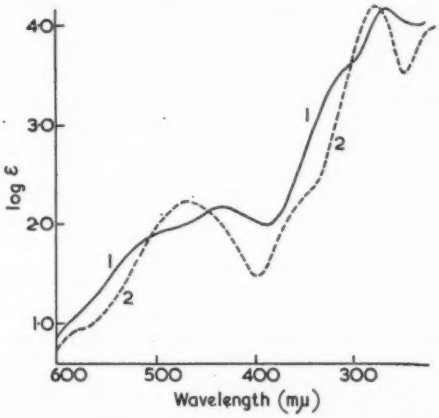
Isomeric forms of the compounds have not been isolated. The infrared spectra indicate that all the monosulphito-compounds have the *cis*-configuration. This evidence is not conclusive, and attempts to resolve the complex ions have not been successful.

[6] Chamberlain and Bailar, *J. Amer. Chem. Soc.*, 1959, **81**, 6412; Baldwin, *J.*, 1961, 471.

Monosulphito-compounds containing the Bidentate Sulphito-group.—A mixture of sodium sulphite and *trans*-[Co en_2Cl_2]Cl in a large excess of water was allowed to evaporate in the dark for about six weeks. Brown-red needles were obtained which had the same empirical formula as the compound (I), *viz.*, Co en_2SO_3,Cl,H_2O. The infrared spectrum of this compound was different from that of any of the complexes discussed above. The compound lost water at 120° without noticeable change in the infrared spectrum. It was soluble in water and behaved therein as a 1 : 1 electrolyte, showed the presence of chloride ions, and was not acidic. Molecular-weight determinations indicated that it was monomeric in aqueous solution.

Addition of sodium perchlorate to an aqueous solution of this compound produced brown-red needles of the composition [Co en_2SO_3]ClO_4, the visible absorption spectrum of which was identical with that of the chloride. Both these compounds must contain a chelated sulphito-group. The molecular-weight determinations on the chloride exclude the possibility of a dimeric cation containing sulphito-bridges.

Addition of aqueous sodium thiocyanate to a solution of the chloride gave brown-red crystals, the infrared spectrum of which showed the presence of thiocyanate ion. An



Visible absorption spectra of (1) [Co en_2SO_3]ClO_4 *and* (2) [Co en_2SO_3,OH_2]ClO_4.

iodide and a nitrite were also obtained. Addition of nitrite to the unidentate sulphito-compounds produced an immediate colour change to bright yellow,[5] owing to the formation of a nitrosulphito-compound [Co en_2SO_3,NO_2][9] (which has been isolated). However, no colour change followed addition of nitrite to a solution of the compound [Co en_2SO_3]Cl; brown-red crystals were isolated on addition of methanol; these contained the nitrite ion, conductivity measurements indicated a 1 : 1 electrolyte, and there was no change in the conductivity or in the visible absorption of an aqueous solution during 2 days.

The unidentate sulphito-compounds showed the yellow colour of the disulphito-anion on the addition of sodium sulphite. No colour change was produced when this reagent was added to a solution of the chloride [Co en_2SO_3]Cl, but the solution became yellow after prolonged boiling.

The visible absorption spectra of [Co en_2SO_3]ClO_4 and [Co en_2SO_3,OH_2]ClO_4 are shown in the figure.

Infrared Absorption Spectra.—The absorption bands due to the sulphito-group were determined by comparison of the spectra of the compounds containing the sulphite group with those of *cis*- and *trans*-[Co en_2Cl_2]Cl. The presence of the sulphito-group increased the intensity of the bands due to the deformation of the NH_2 group of the ethylenediamine. In order to distinguish between these intense NH_2 deformation bands and the

bands due to vibration of the SO_3 group, the amine groups were deuterated. The bands assigned to the sulphito-group showed no shift. The bands due to the sulphito-group are shown in Tables 2 and 3.

TABLE 2. *Frequencies (cm.$^{-1}$) of bands due to the sulphito-group in acidosulphitobis(ethylenediamine)cobalt*(III) *complexes.*

a	b	c	d	e	f
1095s	1068s	1099s	1112s	1117s	1117s
1018w	1020w	1089s	1079s	1075s	1062s
943vs	939vs	980vs	970vs	984vs	972vs
625s	630s	629s	637s	625s	625s

a = *cis*-[Co en$_2$(SO$_3$)$_2$]Na
b = *trans*-[Co en$_2$(SO$_3$)$_2$]Na
c = [Co en$_2$SO$_3$,NCS]^0
d = [Co en$_2$SO$_3$,NH$_3$]Cl
e = [Co en$_2$SO$_3$,Cl]^0
f = [Co en$_2$SO$_3$,OH]^0

TABLE 3. *Frequencies (cm.$^{-1}$) of bands due to the sulphito-group in sulphitobis(ethylenediamine)cobalt*(III) *complexes* [Co en$_2$SO$_3$]X.

X = Cl	1119s	1093s	1036vs	989vs	649m	625s
X = I	1119s	1070s	1042vs	983vs	649m	621m
X = SCN	1117s	1093s	1036vs	988vs	649m	621m

Discussion.—Two formulæ are possible for each of the uni- and bi-dentate sulphito-groups. The pyramidal sulphite ion has the symmetry C_{3v}, which would be effectively unchanged on co-ordination through sulphur (formula a). The number of observed infrared bands agrees with that expected from a group with this type of symmetry [7] and compares well with that found for the co-ordinated sulphato-group.

A cobalt–sulphur bond, which might involve $d\pi$–$d\pi$ bonding,[8] would also explain the marked lability of the unidentate sulphito-complexes. The withdrawal of electrons of the 3*d*-shell of the cobalt would allow attack, either by a water dipole or by an anion.[9] The kinetics of replacement reactions in these complexes is being investigated.

The bidentate sulphito-group may have structure (c) or (d). Structure (d) would involve a three-membered ring which might easily be ruptured. The sulphitobis(ethylenediamine)cobalt(II) compound, however, appears to be stable to water. There is no easy way of converting the bidentate sulphite into the unidentate and *vice versa*, so the bonding of the bidentate and of the unidentate group are probably different in type. It appears likely that the unidentate group is bound to cobalt through sulphur and that the chelate group is bound through two donor oxygen atoms.

EXPERIMENTAL

Visible absorption spectra were measured on a Unicam S.P. 500 spectrophotometer, 10 mm. silica cells being used.

Infrared spectra of solids were measured in Nujol (B.P. grade) mulls between sodium chloride plates, on a Grubb–Parsons G.S.2A double-beam recording spectrometer.

Conductivities were measured with a Philips AC bridge. The cell (constant 1·39) was fitted with bright platinum electrodes.

Chlorosulphitobisethylenediaminecobalt(III) *Monohydrate.*—*trans*-[Co en$_2$Cl]Cl was dissolved in the least volume of water at 30°. The required amount of sodium sulphite, in the least volume of water, was added. On gentle heating, red-brown crystals appeared. The mixture was cooled

[7] Nakamoto, Fujita, Tanaka, and Koboyashi, *J. Amer. Chem. Soc.*, 1957, **79**, 4904.
[8] Craig, Maccol, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.
[9] Ašperger and Ingold, *J.*, 1956, 2862.

and filtered. The crystalline *monohydrate* was washed with methanol and ether (Found: C, 15·2; H, 5·4; S, 9·6; Cl, 10·7. $C_4H_{18}ClCoN_4O_4S$ requires C, 15·35; H, 5·8; S, 10·0; Cl, 11·0%). Drying at 120° for 2 hr. gave the anhydrous *compound* (Found: C, 15·7; H, 5·1; S, 10·7, 11·1. $C_4H_{16}ClCoN_4O_3S$ requires C, 16·3; H, 5·4; S, 10·85%). Concentrated hydrochloric acid converted the following compounds into the same chlorosulphitobisethylenediaminecobalt(III) complex: *cis*-[Co en$_2$(SO$_3$)$_2$]Na, *trans*-[Co en$_2$(SO$_3$)$_2$]Na, [Co en$_2$SO$_3$,NH$_3$]Cl, and [Co en$_2$SO$_3$,OH].

Thiocyanatosulphitobisethylenediaminecobalt(III).—(i) The salt[5] *trans*-[Co en$_2$NCS,OH$_2$]Br$_2$ was dissolved in the least volume of water, and sodium sulphite (required amount) was added. The mixture was heated to the b. p. and placed in the dark overnight. Dark brown needles of the *dihydrate* were filtered off and washed with methanol and ether (Found: C, 17·2; H, 5·7; N, 19·3. $C_5H_{20}CoN_5O_5S_2$ requires C, 17·0; H, 5·7; N, 19·8%).

(ii) The chloride,[5] *cis*-[Co en$_2$NCS,Cl]Cl was dissolved in the least amount of water, and sodium sulphite (required amount) was added. On warming, pale brown needles appeared. The infrared spectrum of this compound was identical with that of the compound prepared as in (i).

(iii) The chlorosulphitobisethylenediaminecobalt(III) complex was dissolved in water, and a saturated solution of sodium thiocyanate was added. On the addition of acetone pale brown crystals appeared; they were filtered off and washed with acetone. Their infrared spectrum was identical with those of the compounds obtained by methods (i) and (ii). These needles are the *trihydrate* (Found: C, 16·3; H, 5·5. $C_4H_{22}CoN_5O_6S_2$ requires C, 16·2; H, 5·9%). The compound is partially ionised in water: $\Lambda = 33{\cdot}5$ ohm^{-1} for a $8{\cdot}6 \times 10^{-4}$M-solution at 25°.

Aquosulphitobisethylenediaminecobalt(III) *Perchlorate.*—The *perchlorate* [Co en$_2$SO$_3$,OH$_2$]ClO$_4$ was prepared by the action of aqueous sodium perchlorate on the complex [Co en$_2$SO$_3$Cl]°. Yellow brown crystals were obtained after a few minutes and were filtered off and washed with ethanol and ether (Found: C, 12·8; H, 5·05. $C_4H_{18}ClCoN_4O_8S$ requires C, 12·8; H, 4·8%). The compound became red at 120° and was then insoluble in water and organic solvents. However, on being left in contact with water it gradually dissolved. The colour of the solution was yellow-brown and the visible absorption spectrum showed the presence of the [Co en$_2$SO$_3$,OH$_2$]$^+$ ion. Analysis of the red *compound* showed that it contained one molecule of water less than [Co en$_2$SO$_3$,OH$_2$]ClO$_4$. The infrared spectrum was clearly different from those containing the chelated sulphito-group. It is possible that a dimerisation or polymerisation occurred, giving compounds which involve bridging sulphito-groups of the type $R_5Co{-}S(O_2){-}O{-}CoR_5$ (Found: C, 13·2; H, 5·0. $C_4H_{16}ClCoN_4O_7S$ requires C, 13·35; H, 4·5%).

Aminosulphitobisethylenediaminecobalt(III) *Chloride.*—Sufficient 2N-ammonia was added to the compound [Co en$_2$SO$_3$,Cl]° to form a solution. The mixture was gently boiled for a few minutes; on cooling, yellow-brown needles of a *chloride* [Co en$_2$SO$_3$,NH$_3$]Cl were precipitated. These were filtered off and washed with methanol and acetone (Found: C, 15·3; H, 6·5; N, 21·2; S, 10·4. $C_4H_{19}ClCoN_5O_3S$ requires C, 15·4; H, 6·15; N, 22·4; S, 10·3%). An aqueous $3{\cdot}84 \times 10^{-3}$M-solution had a molar conductivity of 91 ohm^{-1} at 18·5°. Both the solid and the aqueous solution became bright orange at >60°. On cooling, they revert to their original colour.

Hydroxosulphitobisethylenediaminecobalt(III).—This was prepared from the complex [Co en$_2$SO$_3$,Cl]° by the action of 2N-sodium hydroxide. Methanol, followed by acetone, was added to the mixture and the *complex* [Co en$_2$SO$_3$,OH]° then appeared as golden-yellow plates. It was filtered off and washed with acetone. It is soluble in water and in methanol (Found: C, 15·7; H, 6·8; S, 9·9. $C_4H_{17}CoN_4O_4$ requires C, 15·4; H, 6·7; S, 10·2%). [Co en$_2$SO$_3$,OH] was also prepared by addition of sodium hydroxide to *cis*-[Co en$_2$(SO$_3$)$_2$]Na.

Sulphitobisethylenediaminecobalt(III) *Chloride.*—The chloro-complex *trans*-[Co en$_2$Cl$_2$]Cl was dissolved in a large excess of water, sodium sulphite was added, and the mixture was allowed to evaporate in the dark until red-brown crystals appeared (about 6 weeks). These were filtered off and washed with alcohol and ether. The compound was a *monohydrate* (Found: C, 15·3; H, 6·3; N, 18·1; S, 10·2. $C_4H_{18}ClCoN_4O_4S$ requires C, 15·35; H, 5·8; N, 17·9; S, 10·0%).

Sulphitobisethylenediaminecobalt(III) *perchlorate* was obtained immediately on addition of sodium perchlorate to a solution of the preceding chloride. It formed sparingly soluble orange-brown needles (Found: C, 13·4; H, 4·7; S, 9·2. $C_4H_{16}ClCoN_4O_7S$ requires C, 13·45; H, 4·5; S, 8·9%).

Sulphitobisethylenediaminecobalt(III) *nitrite* was obtained more slowly after addition of sodium nitrite to a solution of the chloride. The orange-brown *monohydrate* was formed

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(Found: C, 14·8; H, 5·7. $C_4H_{18}CoN_5O_6S$ requires C, 14·9; H, 5·6%). The conductivity of its aqueous 5·1 × 10^{-4}M-solution was 102·9 ohm^{-1} at 20°.

Sulphitobisethylenediaminecobalt(III) *iodide* was similarly prepared by use of sodium iodide. The brown-orange crystals of the monohydrate were filtered off and washed, with methanol and ether (Found: C, 11·8; H, 4·5; S, 7·9. $C_4H_{18}CoIN_4O_4S$ requires C, 11·9; H, 4·2; S, 7·9%).

Sulphitobisethylenediaminecobalt(III) *thiocyanate* was similarly prepared by addition of sodium thiocyanate, and formed brown-orange needles of the monohydrate which were filtered off and washed with acetone and ether (Found: C, 18·2; S, 19·7. $C_5H_{18}CoN_5O_4S$ requires C, 18·3; S, 19·7%).

Sodium trans-*Disulphitobisethylenediaminecobalt*(III).—The dichloro-chloride *trans*-[Co en_2Cl_2]Cl was dissolved in a little water and an excess of solid sodium sulphite was added. The mixture was boiled, becoming brown and then bright yellow, and, on cooling, yellow crystals of the *sodium salt* appeared. They were filtered and recrystallised as trihydrate from dilute sodium sulphite solution (Found: C, 11·4; H, 5·4; N, 13·4; S, 15·8. $C_4H_{22}CoN_4NaO_9S_2$ requires C, 11·6; H, 5·3; N, 13·6; S, 15·6%). On drying over calcium chloride the crystals crumbled to a yellow powder which was the anhydrous *salt* (Found: C, 13·5; H, 4·2; S, 17·7. $C_4H_{14}CoN_4NaO_6S_2$ requires C, 13·2; H, 4·4; S, 17·8%).

Sodium cis-*Disulphitobisethylenediaminecobalt*(III).—(i) A saturated solution of sodium sulphite was added to the dithionate, *cis*-[Co $en_2NCS,OH_2]S_2O_6$ prepared by using an ion-exchange column.[3b] The solution became brown and then yellow on warming, and finally a yellow powder appeared. The solid anhydrous *salt* was filtered off, washed with ethanol and ether, and dried over calcium chloride (Found: C, 13·3; H, 3·9; N, 16·15; S, 18·5. $C_4H_{16}CoN_4NaO_6S_2$ requires C, 13·2; H, 4·4; N, 15·6; S, 17·8%).

(ii) A solution of the bromide, *trans*-[Co $en_2NCS,OH_2]Br_2$, prepared by Werner's method,[5] was boiled with a large excess of sodium sulphite until a yellow powder was formed. This was filtered off and washed with methanol and ether. Its infrared and visible absorption spectra were identical with those of the compound prepared as in (i).

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600. *Studies in Relation to Biosynthesis. Part XXIV.* Some Remarks on the Structure of Echinulin.*

By A. J. BIRCH, G. E. BLANCE, S. DAVID, and HERCHEL SMITH.

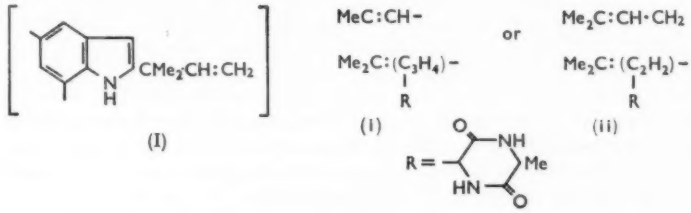
Biological incorporations of [2-^{14}C]mevalonic lactone, [1-^{14}C]acetate, [1-^{14}C]alanine, and [1-^{14}C]glycine into echinulin have independently indicated the presence of three isoprene units and support other aspects of structure and biosynthesis postulated by Quilico's school.[1]

THE traditional method of examining structure–biosynthetic relations has been to determine the structure of a natural product and then to try to rationalise it in terms of possible biosynthetic precursors and reactions.[2] We have now attempted to reverse this process in certain cases by examining with tracer methods the units involved in biosynthesis in order to apply the results to elucidation of structure. This approach becomes possible with an increasing knowledge of biosynthetic routes[3] in cases where incorporation of radioactive precursors can readily be achieved, as with micro-organisms. We now report such an examination of echinulin, produced by *A. echinulatus*[4] or *A. amstelodami*.[5]

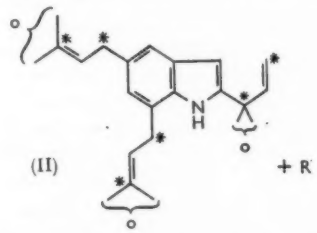
* Part XXIII, Birch, Cameron, and Rickards, *J.*, 1960, 4395.

[1] Cardani, Casnati, Piozzi, and Quilico, *Tetrahedron Letters*, 1959, No. 16, 1.
[2] Robinson, "The Structural Relations of Natural Products," The Clarendon Press, Oxford, 1955.
[3] Birch, *Fortschr. Chem. org. Naturstoffe*, 1957, **16**, 186.
[4] Quilico and Panizzi, *Ber.*, 1943, **76**, 348.
[5] Quilico and Cardani, *Rend. Accad. Lincei*, 1950, **9**, 220.

When this work was begun knowledge of the structure of echinulin, due to the chemical work of Quilico and his colleagues [6] could be summarised in the expression (I).



One isoprene unit is clearly distinguishable, attached in the reverse manner to the 2-position of the indole nucleus, and the presence of the isopropylidene group suggests the possibility of the presence of other isoprene units. Accordingly we fed to *A. amstelodami* the specific terpene precursor [2-^{14}C]mevalonic acid which should place one labelled carbon



atom at one Me position in each unit. Incorporation was of the expected order (4·25%). Acetone was produced by ozonolysis, the derived 2,4-dinitrophenylhydrazone having 35·2% of the activity of the whole molecule, indicating the presence of *three* isoprene units. The most probable skeleton on this basis corresponds to (I, ii) as above, *i.e.*, to (II) with the labelled atoms denoted °.

Kuhn–Roth oxidation of the acetone derivative to acetic acid, and degradation of the latter showed that all of the label was, as expected, on the methyl group. As a further check the organism was fed with Me·$^{14}CO_2Na$, and in this case the acetone derivative contained 16·1%, *i.e.*, about one sixth, of the total activity, corresponding to the expected labelling pattern (II; * = ^{14}C). As required by this pattern all of the activity in the acetone was shown to be on the carbonyl group. To confirm that acetic acid was incorporated only to a notable extent into the isoprene residues one of these was isolated in the known fashion.[6] Hydrogenation, oxidation, and hydrolysis of echinulin gave αα-dimethylvaleric acid which had, as expected, one-third of the activity of the echinulin.

These results all agree with the structure (II) although they do not define the point of attachment of the dioxopiperazine ring. At this stage, in a personal discussion with Professor Quilico (mentioned also by him [1]), we learned that his further chemical work had led to the same conclusion for the skeleton of the molecule.

We have since carried out some further examinations of echinulin biosynthesis. Incorporation of radioactivity from H·$^{14}CO_2H$, was, as expected, very small, and appeared to be random, but incorporation of (±)-[1-^{14}C]alanine and [1-^{14}C]glycine both took place. Hydrolysis of the alanine-derived material gave alanine with 65·8% of the total radioactivity. There is little doubt therefore that, as previously suggested,[1] this is a biosynthetic precursor of the dioxopiperazine ring. Kuhn–Roth oxidation of the alanine-derived echinulin showed that some radioactivity had been randomly incorporated into

[6] Quilico, Piozzi, and Cardani, *Gazzetta*, 1958, **88**, 125, and earlier papers.

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the isoprene unit (probably *via* pyruvate and acetylcoenzyme A). If the usual distribution of the label is assumed, the isoprene units could account for about 19% of the remaining activity. This leaves 14% unaccounted for, in either the glycine or the indole portion. It may be noted that if the latter is derived from shikimic acid, some incorporation of pyruvate (from deamination of alanine) would be expected. Further degradations are necessary to test this possibility.

The glycine-derived echinulin gave rise to alanine with 4·25% of the total labelling (possibly incorporated *via* serine) and the acetic acid from Kuhn–Roth oxidation contained only 1·06% of the total activity. The site of incorporation of the glycine could therefore be either in the dioxopiperazine ring as previously suggested, or in the indole nucleus. Insufficient material was available to decide this point.

By a reaction sequence starting from the potassium salt of echinulin and involving pyrolysis, hydrogenation, and oxidation, Quilico *et al.*[6] obtained a substance $C_{22}H_{35}NO_3$ which was considered to have the nuclear skeleton of (II) lacking the R group. In confirmation we have found that the compound formed from [2-^{14}C]mevalonate-derived echinulin has the same molar activity as the parent, and so must have retained all the labelled carbon atoms.

Clearly, tracer incorporation in this case could have provided valuable structural information. It did, in fact, lead from the partial structure (I) to the more complete (II) independently of the chemical work.

[Added, May 29th 1961.] Professor Quilico informs us [6a] that echinulin is $C_{29}H_{39}N_3O_2$, instead of $C_{28}H_{37}N_3O_2$, and carries the dioxopiperazine ring attached to the 3-position by CH_2. The substance is therefore satisfactorily related biogenetically to tryptophan. Our general conclusions are unaltered; the r.m.a. figures for echinulin and its derivatives should be multiplied by 1·031 and the figures are then a better fit. We had in fact mentioned to Professor Quilico in a personal communication that the tracer results fitted better for a C_{29} than a C_{28} formula.

Experimental

General instructions are as for Part XIII.[7]

Echinulin.—A. amstelodami, from the collection of the Musée Nationale d'Histoire Naturelle, Paris, was sub-cultured for 6 days on Czapek–Dox agar slopes, and then grown on a medium made by adding potassium dihydrogen phosphate to sugar-beet molasses and making up the solution to 1 l. The cultures from 7 l. of medium were harvested after 11 days and the mycelium was dried at room temperature. It was then finely powdered, extracted continuously (Soxhlet) with light petroleum (b. p. 30—40°), and exhaustively extracted with ether (Soxhlet) for 3 days. The precipitate from the ether reservoir recrystallised from ethanol, to give echinulin (4·5 g.) as needles, m. p. 230—242°, spectroscopically identical [8] with a sample from Professor Quilico (Milan).

[^{14}C]*Echinulin.*—The mould was grown as above, the [^{14}C]-precursors being introduced into the culture medium 4 days after inoculation when a mycelial mat had grown. Growth was allowed to continue for a further 6 days and the product isolated. The precursors, amount of culture solution, yields, and incorporations were as follows: Me·$^{14}CO_2Na$(0·3 mc), 900 c.c., 0·78 g., 0·74%; [2-^{14}C]mevalonic lactone (0·05 mc), 600 c.c., 0·55 g., 4·25%; H·$^{14}CO_2Na$ (0·2 mc), 600 c.c., 0·35 g., 0·04%; (±)-[1-^{14}C]alanine (0·25 mc), 600 c.c., 0·51 g., 0·12%; [1-^{14}C]glycine (0·2 mc), 600 c.c., 0·78 g., 0·84%.

Ozonolysis of Echinulin.—Echinulin (0·6 g.) was ozonised [8] in acetic acid (40 c.c.), the ozonide was worked up as usual with zinc powder, and the volatile carbonyl compounds were

[6a] Quilico, personal communication; Casnati, Piozzi, Quilico, and Ricca, *Chimica e Industria*, 1961, 412.

[7] Birch, Massy-Westropp, Rickards, and Smith, *J.*, 1958, 360.

[8] Cardani, Casnati, Cavelleri, and Quilico, *Rend. Accad. Lincei*, 1958, **24**, 488.

swept by nitrogen into Brady's reagent. The 2,4-dinitrophenylhydrazones were separated by chromatography on bentonite—kieselguhr with ether containing 6% of ethanol as eluent.[9] The band corresponding to acetone 2,4-dinitrophenylhydrazone gave a product, m. p. 126—127° undepressed by the authentic material.

[^{14}C]Echinulin (r.m.a. $1{\cdot}0 \times 10^5$) from Me·$^{14}CO_2Na$ gave acetone 2,4-dinitrophenylhydrazone (r.m.a. $1{\cdot}61 \times 10^4$). Kuhn–Roth oxidation of the latter to acetic acid and degradation of this in the usual manner [10] gave barium carbonate from Me with r.m.a. 0·0 and from CO_2H with r.m.a. $1{\cdot}62 \times 10^4$.

[^{14}C]Echinulin (r.m.a. $2{\cdot}66 \times 10^5$) from [2-^{14}C]mevalonic lactone gave acetone 2,4-dinitrophenylhydrazone (r.m.a. $9{\cdot}36 \times 10^4$). Kuhn–Roth oxidation of the latter and degradation of the resulting acetic acid as above gave barium carbonate from Me with r.m.a. $4{\cdot}56 \times 10^4$ (Calc. for three equally labelled methyl groups, $4{\cdot}685 \times 10^4$) and from CO_2H with r.m.a. 0·0.

Oxidation of Hexahydroechinulin by Peracetic Acid.—[^{14}C]Hexahydroechinulin (r.m.a. $1{\cdot}00 \times 10^3$) from Me·$^{14}CO_2Na$ was oxidised, and the product hydrolysed as previously described [6] to αα-dimethylvaleric acid which was converted in the usual manner into the 4-phenylphenacyl ester m. p. 85—86° (r.m.a. $3{\cdot}42 \times 10^4$. Calc. for three equally labelled isoprenoid units, r.m.a. $3{\cdot}33 \times 10^4$).

Pyrolysis of the Potassium Derivative of Echinulin.—[^{14}C]Echinulin (5 g.; r.m.a. $2{\cdot}66 \times 10^5$), derived from [2-^{14}C]mevalonic lactone, was converted into the potassium derivative and pyrolysed as previously described.[11] Oxidation of the product in the known manner [6] with hydrogen peroxide gave the substance $C_{23}H_{37}NO_3$, m. p. 119—121° (r.m.a. $2{\cdot}69 \times 10^5$).

Kuhn–Roth Oxidations.—Oxidation of echinulin gave acetic acid in 55% yield (for 4*C*-Me groups). The acid was degraded as before to barium carbonate from the Me and CO_2H groups. [^{14}C]Echinulin (r.m.a. $4{\cdot}80 \times 10^4$) from H·$^{14}CO_2Na$ gave barium carbonate from Me with r.m.a. $1{\cdot}46 \times 10^3$ and from CO_2H with r.m.a. $9{\cdot}34 \times 10^3$. [^{14}C]Echinulin (r.m.a. $7{\cdot}15 \times 10^4$) from (±)-[1-^{14}C]alanine gave barium carbonate from Me with r.m.a. $2{\cdot}66 \times 10^2$ and from CO_2H with r.m.a. $1{\cdot}16 \times 10^3$. [^{14}C]Echinulin (r.m.a. $1{\cdot}34 \times 10^5$) from [1-^{14}C]glycine gave barium carbonate from Me with r.m.a. $3{\cdot}66 \times 10^2$ and from CO_2H with r.m.a. $1{\cdot}06 \times 10^3$.

Hydrolysis of Hexahydroechinulin.—Hydrolysis as previously described [12] gave alanine, which was converted in the usual manner into the picrolonate. [^{14}C]Hexahydroechinulin (r.m.a. $7{\cdot}07 \times 10^4$) from (±)-[1-^{14}C]alanine gave alanine (r.m.a. $4{\cdot}65 \times 10^4$) [picrolonate, m. p. 214—215° (r.m.a. $4{\cdot}72 \times 10^4$)]. [^{14}C]Hexahydroechinulin (r.m.a. $7{\cdot}07 \times 10^4$) from [1-^{14}C]glycine gave alanine (r.m.a. $5{\cdot}69 \times 10^3$) [picrolonate, m. p. 214—215° (r.m.a. $5{\cdot}54 \times 10^3$); lit.,[13] 215°].

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Department of Chemistry, University of Manchester.
Laboratoires de Chimie Biologique,
Faculté des Sciences de Nancy.

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[9] Elvidge and Whalley, *Chem. and Ind.*, 1955, 589; Braddock, Garlow, Grim, Kirkpatrick, Pease, Pollard, Price, Reissmann, Rose, and Willard, *Analyt. Chem.*, 1953, **25**, 301.
[10] Cornforth, Hunter, and Popjak, *Biochem. J.*, 1953, **54**, 597.
[11] Quilico, Cardani, and Piozzi, *Gazzetta*, 1955, **85**, 3.
[12] Quilico, Cardani, and Piozzi, *Gazzetta*, 1956, **86**, 211.
[13] Levene and van Slyke, *J. Biochem.*, 1912, **12**, 127.

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601. *The Magnetic Properties of Some* d^4*-Complexes.*

By A. Earnshaw, B. N. Figgis, J. Lewis, and R. D. Peacock.

The magnetic susceptibilities of a number of complexes of rhenium, ruthenium, osmium, and iridium of the d^4-electronic configuration have been measured between 80° and 300° K. The results are discussed with reference to the relation between the ligand fields, the interelectronic repulsions, and the spin–orbit coupling constants of the ions concerned. It is found that the free-ion values of those parameters account for the results.

Recently a better understanding of the reasons for the difference between the magnetic behaviour of the first transition-series ions on the one hand, and the second- and third-series ions on the other, has been achieved.[1–5] It has been realised that both the ligand fields and the spin–orbit coupling are greater in the later transition series, and that this invalidates the assumptions which simplify the magnetic properties of most of the complexes of the first transition-series elements. The larger ligand fields lead to complexes that are always of the spin-paired type. In the presence of large spin–orbit coupling the theory which describes the magnetic properties of $4d^4$- and $5d^4$-ions cannot be simplified as it can for $3d^4$-configuration, and magnetic behaviour has to be considered separately for each ion, or perhaps even for each complex.

The present paper presents measurements of the variation of the magnetic susceptibility with temperature for a number of second and third transition-series complexes. The results obtained for d^4-configurations are considered first, being the most comprehensive. The results for the d^3-configuration are given in the next paper. A preliminary report has already been given.[2] The complexes studied were chosen, so far as possible, to have six equivalent ligands surrounding the central metal ion, for only then can the environment

Table 1. *Estimated spin–orbit coupling constants* (ζnd) *and interelectronic repulsion parameters for the second and third transition-series ions of* d^4*-configuration.*[8]

	Ion	ζnd (cm.$^{-1}$)	$3F_2 + 20F_4$; $3B + C$ (cm.$^{-1}$)		Ion	ζnd (cm.$^{-1}$)	$3F_2 + 20F_4$; $3B + C$ (cm.$^{-1}$)
$4d^4$	Ru^{IV}	1400	5000	$5d^4$	Os^{IV}	4000	3500
$5d^4$	Re^{III}	2500	3250	$5d^4$	Ir^{V}	5500	3650

F_2 and F_4 are the Condon–Shortley parameters or interelectronic repulsion, B and C are those due to Racah.

of the central ion be, in the first approximation at least, of cubic symmetry. The effect of ligand fields of symmetry lower than cubic on the magnetic properties of the ions will be considered elsewhere. However, as found for the t^5_{2g}-configuration, ligand fields of low symmetry whose magnitude is of the same order as, or less than, the spin–orbit coupling constant do not much affect the average magnetic moment of the t^4_{2g}-configuration, so that we may largely neglect them in dealing with regular octahedral complexes of the second and third transition series.[6]

The ligand field parameter, $10Dq$, which measures the separation between the t_{2g}- and the e_g-orbital subsets in the ligand field from an octahedral arrangement of co-ordinating groups, is known to be consistently ~50% larger for 4*d*- than for 3*d*-electron configurations. In the 5*d*-shell, $10Dq$ is ~70% larger than in the 3*d*-shell.[7] On the other hand it seems

[1] Figgis, *J. Inorg. Nuclear Chem.*, 1958, **8**, 482.
[2] Figgis, Lewis, Nyholm, and Peacock, *Discuss. Faraday Soc.*, 1959, **26**, 103.
[3] Griffith, *Discuss. Faraday Soc.*, 1959, **26**, 173.
[4] Kamimura, Koide, Sekiyama, and Sugano, *J. Phys. Soc. Japan*, 1960, **15**, 1264.
[5] Fred, Goodman, Moffitt, and Weinstock, *Mol. Phys.*, 1959, **2**, 109.
[6] Figgis, unpublished work.
[7] Jørgensen, 10th Conseil de l'Institute International de Chimie, Solvay, 1956, p. 355.
[8] Dunn, personal communication.

that spin-pairing energies are smaller for the 4*d*- and 5*d*- than for the 3*d*-shell, because of reduced interelectronic repulsion terms. Consequently, although complexes of both the spin-free type (where the spin-pairing energy is greater than the ligand field) and the spin-paired type (where the converse is true) exist for many first transition-series ions, only spin-paired complexes are known for the later two series. For the second and third transition-series ions spin–orbit coupling constants are undoubtedly larger than in the first series. Table 1 gives estimated spin–orbit coupling and interelectronic repulsion parameter values for 4*d*- and 5*d*-ions which are pertinent to the present work.[8]

It is believed that in transition-metal complexes, particularly those of the spin-paired type, the electrons in t_{2g}-orbitals may be delocalised on to the ligand atoms for a part of their time. This phenomenon has been allied with π-bonding between the metal and the ligand atoms.[9,10] Its effect on the magnetic properties of the t_{2g}-electrons has been described by supposing that the orbital angular momentum associated with the subset is lost for the fraction of time spent on the ligands. Accordingly [11] the orbital angular momentum operator may be reduced by a factor, k. k has been estimated to lie mostly between ~0·7 and 1.

The Magnetic Behaviour of the t^4_{2g}*-Configuration.*—Kotani [12] showed that the spin-paired configuration of d^4 in the ligand field from an octahedral distribution of ligand atoms t^4_{2g}, has, under the action of a modified form of Russell–Saunders coupling within the t_{2g} subset, a $^3T_1$ term lying lowest. Spin–orbit coupling was found to lift the degeneracy of this term and the magnetic susceptibility of the system is

$$\chi_M = \frac{N\beta^2}{3kT} \cdot \frac{48 + (x - 18)\exp(-x/2) + (5x - 30)\exp(-3x/2)}{2x[1 + 3\exp(-x/2) + 5\exp(-3x/2)]},$$

with $x = \zeta/kT$. When x is very much greater than unity ($\zeta \gg kT$) only the lowest non-degenerate level of the system is occupied at available temperatures, and the susceptibility arises only from the second-order Zeeman effect between this and higher levels, and is of the temperature-independent type.

Then: $$\chi_M = 24N\beta^2/\zeta.$$

When x is of the order of unity ($\zeta \sim kT$) the dependence of the susceptibility on temperature is complicated. For Ru^{IV} $[(NH_4)_2RuCl_6]$ ($x \simeq 8$ at 300° K) the dependence of the susceptibility on temperature has been found to be small, and it is absent for Os^{IV} (K_2OsBr_6) ($x \simeq 16$ at 300° K). For Mn^{III} spin-paired $[K_3Mn(CN)_6]$ ($x \simeq 2$ at 300° K) the susceptibility varies with temperature in a somewhat unusual manner. These results may be explained, in the first approximation at least, on the basis of this theory. However, as pointed out in the preliminary communication,[2] the values which it is necessary to assign to ζ' * in order to obtain the observed susceptibilities of the Ru^{IV}, Os^{IV}, and other isoelectronic ions in complexes are considerably higher than expected on other grounds. This is surprising because, on account of the delocalisation of the t_{2g} electrons on to the ligand atoms, it is generally accepted that ζ' is likely to be lower in the complex than in the free ion.

Griffith [13] improved Kotani's theory by introducing the factor k into the matrix elements of orbital angular moment, thus allowing for the effects of t_{2g}-electron delocalisation, so that the magnetic moment operator is $\mu = (kL + 2S)\beta$ rather than $(L + 2S)\beta$. He also

* We reserve ζ for the free-ion value of the spin–orbit coupling, and the primed symbol, ζ', for the quantity in the complex, but not including the effective reduction resulting from delocalisation. It should be noted that ζ', the spin–orbit coupling constant for use within the t_{2g} set, is not quite equivalent even [after allowance for the factor ($\pm 2S$)] to the quantity λ' which has been used to denote the effective spin–orbit coupling constant between the t_{2g} and e_g sets.[10]

[9] Dunn, *J.*, 1959, 623.
[10] Owen, *Proc. Roy. Soc.*, 1955, *A*, **227**, 183.
[11] Stevens, *Proc. Roy. Soc.*, 1953, *A*, **219**, 542.
[12] Kotani, *J. Phys. Soc. Japan*, 1949, **4**, 293.
[13] Griffith, *Trans. Faraday Soc.*, 1958, **54**, 1009.

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demonstrated the relation between the configurations (t^n_{2g}) and p^n which allows the properties of the former to be obtained from those of the latter by the substitution of $-L$ for L in the magnetic moment operator. The expression for the susceptibility for $\zeta' \gg kT$ then becomes

$$\chi_M = 8N\beta^2(2 + k)^2/3k\zeta'.$$

However, this treatment makes little difference to the values of ζ' which must be invoked to account for the experimental susceptibilities of the ions concerned.

We suggested that a way out of the difficulty might be to take into consideration the fact that when ζ' is large it may no longer be negligibly small compared with the electrostatic repulsions between the t_{2g} electrons, *i.e.*, that a form of coupling intermediate between Russell–Saunders and $j.j$ may be required.[2] It was estimated that, in intermediate coupling, the observed susceptibilities for $4d^4$- and $5d^4$-ions could be accounted for with very reasonable values of ζ'. Griffith [3] has completed the calculations for the susceptibility of t^4_{2g} with $\zeta' \gg kT$, based on its equivalence to p^2. He finds that

$$\chi_M = \frac{2N\beta^2(1 + \cos\theta)\,(2 + k)^2}{3\delta\,(8^{-1}\tan\theta - 1 + \sec\theta)}, \qquad \ldots\ldots (1)$$

with $\delta = \frac{1}{2}(15B + 5C + \zeta')k$ and $\tan\theta = 2^{\frac{1}{2}}\zeta'/\delta$. [It is presumed that the interelectronic repulsion parameters are reduced in the complex by the same factor, k, as is ζ', and eqn. (1) differs in this way from the expression given by Griffiths.]

The magnetic moment for t^4_{2g} has been worked out also in intermediate coupling for $\zeta' \gg kT$ by Kamimura *et al.*,[4] but no allowance for the effects of electron delocalisation was made. With reasonable estimates of interelectronic repulsion parameters and ζ', it has been possible to account for the observed moments of some compounds of Ru^{IV}, Os^{IV}, and Ir^{V}. The results of Kamimura *et al.* are not presented in a form which is convenient for use when ζ' is very much greater than kT. However, for this case, an investigation of theory shows that the only contribution to the susceptibility is from the second-order Zeeman effect between the ground level and one non-degenerate higher level. Consequently, the susceptibility can be shown of the form

$$\chi_A = \chi^0{}_A \tanh\,(a/2kT) \qquad \ldots\ldots (2)$$

where $\chi^0{}_A$ is the limiting susceptibility at zero temperature, and a is the separation between the ground and the higher level.

Results.—The results of the measurements of the magnetic susceptibilities of nineteen complexes of Re^{III}, Ru^{IV}, Os^{IV}, and Ir^{V} between 80° and 300° K are set out in Table 3. In Figs. 1—5, the susceptibility is plotted against temperature. For the ruthenium complexes the solid lines are plots of eqn. (2) for the values of a and $\chi^0{}_A$ given in Table 2. For the other

TABLE 2. (a) *Magnetic properties, at* 300° K, *of the complexes studied.*

Compound	$10^6\chi_A$ (c.g.s./mole)	μ_{eff} (B.M.)	$10^6\chi^0{}_A$	Compound	$10^6\chi_A$ (c.g.s./mole)	μ_{eff} (B.M.)	$10^6\chi^0{}_A$
K_2RuF_6	3380	2·86	3960	Cs_2OsF_6	935	1·50	950
K_2RuCl_6	3018	2·70	3700	K_2OsCl_6	941	1·51	940
$(NH_4)_2RuCl_6$	3150	2·76	3620	Cs_2OsCl_6	1162	1·67	1200
Rb_2RuCl_6	3750	3·01	4280	K_2OsBr_6	603	1·21	610
K_2RuBr_6	3322	2·84	3570	Cs_2OsBr_6	1285	1·76	1320
Rb_2RuBr_6	3270	2·81	3420	K_2OsI_6	788	1·38	820
$ReD_2Cl_2(ClO_4)$ *	1908	2·14	1960	Cs_2OsI_6	1128	1·65	1150
$ReD_2Br_2(ClO_4)$	1690	2·02	1664	$KIrF_6$	670	1·27	712
$ReD_2I_2(ClO_4)$	1260	1·74	1260	$CsIrF_6$	687	1·29	700
K_2OsF_6	713	1·31	713				

* D = *o*-phenylenebisdimethylarsine.

(b) *Values of a, from eqn.* (2), *for the complexes of ruthenium.*

Compound	K_2RuF_6	K_2RuCl_6	$(NH_4)_2RuCl_6$	Rb_2RuCl_6	K_2RuBr_6	Rb_2RuBr_6
a (cm.$^{-1}$)	508	486	480	546	664	660

Plots of χ_{Metal} *against temperature.*

FIG. 1. *A*, Rb_2RuCl_6; *B*, K_2RuCl_6; *C*, $(NH_4)_2RuCl_6$.

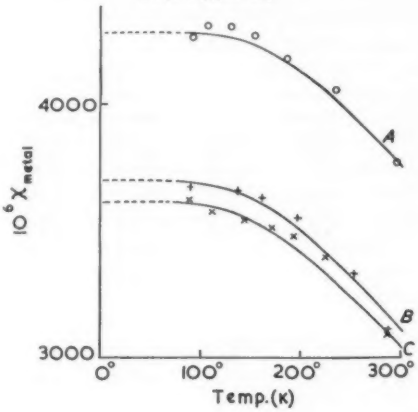
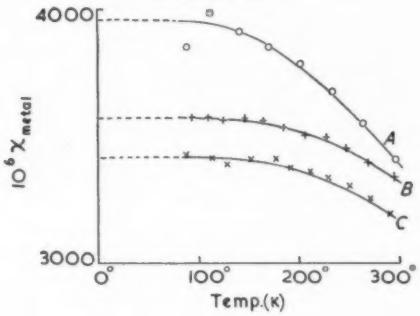


FIG. 2. *A*, K_2RuF_6; *B*, K_2RuBr_6; *C*, Rb_2RuBr_6.



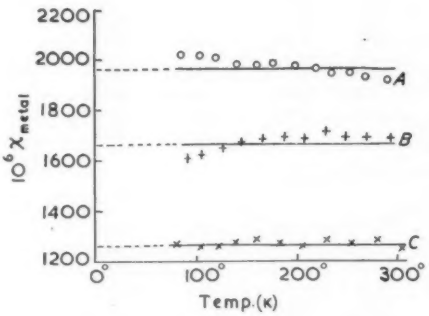


FIG. 3. *A*, $ReD_2Cl_2ClO_4$; *B*, $ReD_2Br_2ClO_4$; *C*, $ReD_2I_2ClO_4$.

FIG. 4. *A*, Cs_2OsBr_6; *B*, Cs_2OsF_6; *C*, K_2OsF_6; *D*, $CsIrF_6$; *E*, K_2OsBr_6.

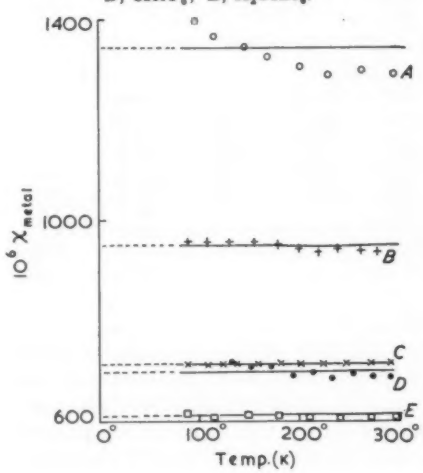
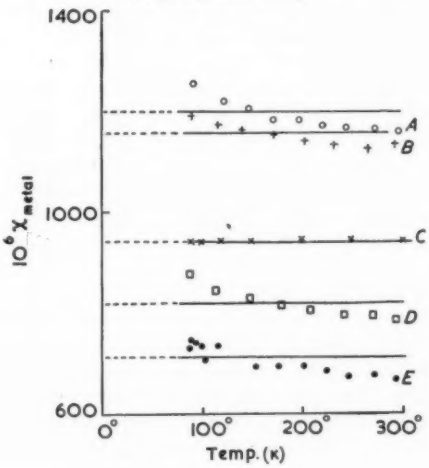


FIG. 5. *A*, Cs_2OsCl_6; *B*, Cs_2OsI_6; *C*, K_2OsCl_6; *D*, K_2OsI_6; *E*, $KIrF_6$.



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complexes ζ' is so large that $\tanh(a/2kT)$ is unity and the plot is of χ^0_A. The magnetic susceptibilities and moments at 300° K are also summarised in Table 2.

TABLE 3. *Magnetic susceptibilities of the compounds studied.*

(Temperatures are in °K, susceptibilities in 10^{-6} c.g.s./mole.)

K_2RuF_6		K_2RuCl_6		$(NH_4)_2RuCl_6$		Rb_2RuCl_6		K_2RuBr_6	
Temp.	Ru	Temp.	Ru	Temp.	Ru	Temp.	Ru	Temp.	Ru
297·0°	3397	288·1°	3112	288·1°	3189	296·1°	3765	296·5°	3338
264·4	3541	254·3	3328	226·4	3399	234·8	4057	270·0	3396
234·2	3670	197·0	3549	194·3	3474	186·2	4169	248·5	3448
203·0	3777	162·5	3629	172·1	3505	154·5	4264	228·8	3486
172·8	3856	138·4	3654	145·0	3540	131·0	4306	207·2	3507
141·8	3914	91·3	3652	111·6	3577	108·4	4303	187·2	3535
113·5	3985			92·0	3616	92·7	4266	166·2	3556
88·8	3853							147·3	3562
								125·8	3564
								110·0	3576
								95·7	3573

Rb_2RuBr_6		$ReD_2Cl_2(ClO_4)$ *		$ReD_2Br_2(ClO_4)$ *		$ReD_2I_2(ClO_4)$ *		K_2OsF_6	
Temp.	Ru	Temp.	Re	Temp.	Re	Temp.	Re	Temp.	Os
292·5°	3194	290·7°	1919	293·6°	1687	304·1°	1247	291·0°	713
271·8	3249	269·4	1936	268·9	1691	279·6	1282	271·7	713
252·9	3299	252·8	1954	228·6	1710	254·3	1270	245·7	713
231·1	3337	235·8	1954	207·8	1687	230·3	1283	224·0	713
211·7	3359	219·2	1963	187·6	1695	206·8	1259	200·9	713
192·2	3377	199·1	1963	166·9	1684	183·1	1270	182·3	713
154·2	3412	178·3	1981	146·7	1675	161·1	1282	159·2	713
129·3	3389	160·9	1976	127·1	1654	138·2	1270	138·0	713
114·3	3413	141·2	1976	106·4	1621	121·5	1259	124·1	713
88·8	3433	120·7	2003	93·0	1610	105·4	1259	109·8	713
		104·0	2017			79·4	1270	88·9	713
		87·4	2012						

* D = *o*-phenylbisdimethylarsine.

Cs_2OsF_6		K_2OsCl_6		Cs_2OsCl_6		K_2OsBr_6		Cs_2OsBr_6	
Temp.	Os	Temp.	Os	Temp.	Os	Temp.	Os	Temp.	Os
278·5°	937	300°	941	296·5°	1162	295·3°	603	295·4°	1285
261·7	937	250	941	272·4	1166	272·4	604	264·4	1293
240·0	934	200	941	244·5	1171	239·6	604	231·3	1285
220·1	937	150	941	220·6	1175	209·5	604	202·4	1300
200·7	940	120	941	196·6	1188	179·2	610	171·1	1327
179·8	950	100	941	171·1	1188	148·9	609	146·8	1342
155·6	957	90	941	147·1	1209	115·0	609	115·6	1365
131·0	954			122·6	1222	87·4	617	98·0	1392
108·7	957			91·0	1257				
89·8	957								

K_2OsI_6		Cs_2OsI_6		$KIrF_6$				$CsIrF_6$	
Temp.	Os	Temp.	Os	Temp.	Ir	Temp.	Ir	Temp.	Ir
296·2°	789	294·4°	1132	294·3°	670	104·3°	708	289·1°	687
269·5	794	267·1	1128	272·5	678	98·9	732	272·3	687
241·9	798	233·3	1132	246·8	673	94·1	739	253·0	691
208·4	808	202·7	1142	224·1	685	91·9	744	233·0	687
179·9	818	173·0	1153	201·6	694	89·5	755	213·9	695
149·8	827	141·9	1163	177·2	694			193·1	691
114·3	844	116·3	1177	154·7	694			172·0	706
88·4	877	90·7	1191	115·7	735			151·9	709
								133·1	713

DISCUSSION

Ruthenium.—As pointed out by Griffith,[3] the application of eqn. (1) to the estimated values of the parameters of spin–orbit coupling and interelectronic repulsion for Ru^{IV} (free ion) [$\zeta = 1400$ cm.$^{-1}$; $\delta = 13{,}200$ cm.$^{-1}$] leads to a susceptibility of 3590×10^{-6} c.g.s./mole at zero temperature. To this figure a small contribution from the second-order Zeeman effect with higher-lying ligand field levels, probably about 60×10^{-6} c.g.s./mole,

should be added, giving a total of 3650×10^{-6} c.g.s./mole. If ζ' is less than ζ, or if k is less than 1·00, this figure is increased—to 5400×10^{-6} c.g.s./mole if $k = 0{\cdot}7$. It may be compared with the figure of 4435×10^{-6} c.g.s./mole obtained from Kotani's theory applied in the same way. The values of χ^0_{Ru} listed in Table 2 range from 3420 to 4280×10^{-6} c.g.s./mole. It seems, then, that the low-temperature susceptibility of the ruthenium complexes may be very satisfactorily accounted for, in the first approximation at least, on the intermediate coupling scheme and by employing spin–orbit coupling and inter-electronic repulsion parameters little if any lower than for the free ion. In the theory the only mechanism for differences appearing between individual complexes lies in the variation of the constant k. It might be expected that k should decrease in the series of ligands F, Cl, Br, and consequently, that χ^0_{Ru} should rise in that order. However, no correlation between the value of χ^0_{Ru} and the halogen ligand atom can be seen, and the difference between values for the same halogen with different cations may be larger than that between different halogens. From the theory of Kamimura *et al.*[4] it may be calculated, by employing $\zeta' = 1400$ cm.$^{-1}$ and $3B + C = 5000$ cm.$^{-1}$ (obtained from $\delta = 13{,}200$ cm.$^{-1}$) that the level (W_1) with which the second-order Zeeman effect is developed by the ground level (W_3) lies about 900 cm.$^{-1}$ higher. Accordingly, the temperature-dependence of the magnetic susceptibility of the ruthenium complexes should obey the law $\chi_{Ru} = \chi^0_{Ru} \tanh (450/kT)$, *i.e.*, $a = 900$ cm.$^{-1}$. However, from Table 3 this is obviously not so. Figs. 1 and 2 show that the susceptibilities are of the form required by eqn. (2) to a fair degree of accuracy, but the values of a required are too low, by about a factor of 2, for all the compounds. The presence of ligand-field components of symmetry lower than cubic could probably lower the W_1–W_3 separation (a) which was, of course, derived on the basis of a field of cubic symmetry, without much affecting the susceptibility. However, if this is the cause of the reduction, it is remarkable that the low symmetry fields act in the same direction and to much the same amount for each of the six complexes.

Rhenium.—If we assume the free-ion parameters $\zeta = 2500$ cm.$^{-1}$ and (estimated by comparison with Griffith's values[3] for other ions) $3B + C = 3250$ cm.$^{-1}$ for Re^{III}, application of eqn. (1) gives a susceptibility of 1640×10^{-6} c.g.s./mole for χ^0_{Re}. A correction for the second-order Zeeman effect with higher ligand-field levels, of 60×10^{-6} c.g.s./mole, increases this to 1700×10^{-6} c.g.s./mole. The spin-orbit coupling is so large that the susceptibility is not expected to vary with temperature over the range studied. The complexes of rhenium studied differ from those of the other ions in that there are not six equivalent ligand atoms surrounding the central metal atom; consequently, since the ligand field produced by the two halogen atoms will differ markedly from those of the four arsenic atoms, it must be expected that the ligand field experienced by the rhenium atom departs a good deal from cubic symmetry. The values of χ^0_{Re} observed lie between 1960 and 1260×10^{-6} c.g.s./mole and decrease as the atomic number of the halogen atom involved increases. This range includes the value predicted by the theory for a symmetrical rhenium ion. However, it is much larger than that which can be obtained by modifying the theory by reducing k. The temperature-independence of the susceptibility required by the large spin–orbit coupling is nevertheless observed.

Osmium.—The free-ion parameters are $\zeta = 4000$ cm.$^{-1}$ and $3B + C = 3500$ cm.$^{-1}$. From eqn. (1), χ^0_{Os} is calculated to be 880 cm.$^{-1}$, which is increased to 940×10^{-6} c.g.s./mole by the second-order Zeeman effect with higher ligand-field levels. Again, the large spin–orbit coupling requires that the susceptibility be independent of temperature over the range studied. The susceptibilities were found to range from 600 to 1350×10^{-6} c.g.s./mole, and, while several of them are independent of temperature within experimental error, others change with temperature by amounts which are well outside that error. For the compounds of the latter type, obviously, the value to be chosen for χ^0_{Os} is ambiguous. The mean value of χ_{Os} was taken to be χ^0_{Os}. Where the susceptibility varies with temperature it is higher at lower temperatures; consequently, it is tempting to ascribe the variation to the presence of a paramagnetic impurity obeying a Curie law. The presence

of a very small amount of the ion OsX_6^{3-}, whose effect on the analytical results would be negligible, could account for the phenomenon. For this reason the method of choosing χ^0_{Os} may not be the best; perhaps the high-temperature limit might be better. Nevertheless, the fact remains that the values found for χ^0_{Os} differ by a factor of more than two. While the range of values found spans the value predicted by theory, there seems to be no way in which the theory can be modified to account for such a range The problem is more difficult than for the rhenium complexes, for it is expected that the ligand field cannot depart much from cubic symmetry. The susceptibilities are independent of temperature and we are investigating the possibility that magnetic exchange could be consistent with this and responsible for the range of χ^0_{Os} found. No correlation between χ^0_{Os} and the halogen involved or the cation is apparent.

Iridium.—If the free-ion parameters are taken to be $\zeta = 5500$ cm^{-1} and $3B + C = 3650$ cm^{-1}, eqn. (1) predicts that χ^0_{Ir} is 590×10^{-6} c.g.s./mole. The second-order Zeeman effect contribution from higher ligand-field levels increases this to 650×10^{-6} c.g.s./mole. The susceptibility is expected to be independent of temperature. The complexes studied are confined to the fluorides; both have χ^0_{Ir} close to 700×10^{-6} c.g.s./mole, and χ_{Ir} is essentially independent of temperature.

Experimental.—The preparation of the fluoride complexes has been described elsewhere. The remaining halide complexes were prepared and analysed by standard methods. The authors are indebted to Dr. J. E. Fersusson for loan of the rhenium complexes. The measurements of magnetic susceptibility were performed on equipment described previously.[14] The accuracy of the measurement of the absolute susceptibilities of the substances was 2—3%; that of the relative susceptibilities of the same compound at different temperatures was about $\pm 10 \times 10^{-6}$ c.g.s./mole for the rhenium, osmium, and iridium complexes, and about $\pm 20 \times 10^{-6}$ c.g.s./mole for the ruthenium complexes.

The authors thank Dr. F. Mabbs for measurement of the susceptibilities of the rhenium compounds and Dr. T. M. Dunn for help with the estimation of the free-ion spin–orbit coupling and interelectronic repulsion parameters.

William Ramsay and Ralph Forster Laboratories,
University College, Gower Street,
London, W.C.1.

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[14] Figgis and Nyholm, *J.*, 1959, 331.

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602. *The Magnetic Properties of Some* d^3*-Complexes.*

By B. N. Figgis, J. Lewis, and F. E. Mabbs.

The magnetic properties of twenty-one complexes of chromium, molybdenum, rhenium, osmium, and iridium have been measured between 80° and 300° K. The results are discussed with reference to the relation between the ligand fields, the interelectronic repulsions, and the spin–orbit coupling of the ions, and to the magnetic exchange between the ions. The results may be accounted for with reasonable values of the parameters after the fourth of these effects has been allowed for.

The rôle which ligand fields, spin–orbit coupling, and interelectronic repulsions play in determining the magnetic properties of transition-metal complexes was outlined in the preceding paper. For the d^4-complexes considered it appeared that consideration of these three quantities alone was sufficient. However, in the case of the d^3-configuration it is necessary to consider also the effects of magnetic exchange interaction.

It has long been known that in many first transition-series compounds where linear bond arrangements of the form M–L–M occur (L is a ligand atom, particularly oxygen or

fluorine) the electron spins on the two metal atoms (M) may interact through the agency of L, and signs of magnetic interaction are found. These are usually antiferromagnetic in nature. However, it appears that in the second and third transition-series ions, where a greater degree of π-bonding occurs, accompanied by an increased chance of finding the magnetic electrons on the ligand atoms, antiferromagnetic coupling may be transmitted by bonding arrangements such as M–L–L–M.[1] Consequently, antiferromagnetic interactions have been detected in these series in compounds which would normally have been expected to be magnetically dilute. In particular, it is known that the interactions are possible between the metal atoms encased in an octahedron of halogen ligand atoms, as, for instance, in $[IrCl_6]^{2-}$. The possibility of magnetic exchange must, then, be borne in mind when considering the magnetic properties of complexes of the type which we have studied. The presence of magnetic interactions is found to be particularly prominent in the hexahalogen complexes of quadrivalent rhenium, and we have attempted to find the magnetic properties of this ion in the absence of the interactions.

Frequently, when dealing with compounds in which magnetic exchange occurs and which obey the Curie–Weiss law, the magnetic moment is calculated from the equation

$$\mu'_{\text{eff.}} = 2{\cdot}84[\chi_A(T + \theta)]^{\frac{1}{2}}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The use of this expression is based on the fact that many theories of antiferromagnetism predict that the Curie–Weiss law should hold at temperatures very much greater than the Curie temperature (T_c).[2] Although the Curie–Weiss law may hold for a limited range of temperature immediately above T_c it is not correct to employ in eqn. (1) the Weiss constant evaluated from such a range of temperature. Consequently, when dealing with temperature measurements extending from 80° to 300° K, the use of eqn. (1) is not justified if the Weiss constant exceeds, say, 30°, because the theories of antiferromagnetism predict that T_c should be of the order of θ.

The Magnetic Properties of the d^3*-Configuration.*—Provided that spin-orbit coupling can be regarded as a small perturbation of the ligand field or interelectronic repulsions, the magnetic properties of the d^3-configuration in a complex of octahedral stereochemistry is simple. A $^4A_2$ (t^3_{2g}) term lies lowest; the moment differs from the spin-only value for three unpaired electrons (3·88 B.M.) by the factor

$$(1 - 4\lambda''/10Dq) * \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

due to mixing in of the $^4T_1$ term into the $^4A_2$ through spin-orbit coupling.[3] The moment therefore is independent of temperature. The presence of a ligand-field component of symmetry lower than cubic can cause the moment to vary with temperature, as the spin degeneracy of the $^4A_1$ term is then lifted (zero field splitting), but this normally only occurs at very low temperatures.[4]

In the case of ions with large spin–orbit coupling it is necessary to consider an intermediate coupling scheme rather than the simple Russell–Saunders coupling scheme. As a result of the equivalence of the matrices for t^3_{2g} with those of p^3, it is possible to see the main features of the t^3_{2g} in intermediate coupling from the diagram given for p^3 by Condon and Shortley.[6] The lowest ($^4A_2$) level remains four-fold degenerate ($J = 3/2$) throughout the transition to j . j coupling but interacts with a higher level, also with $J = 3/2$. The result of this, if the coupling is still largely of the Russell–Saunders type, is to " dilute " the $^4A_2$

* By λ'' we imply λ reduced by electron delocalisation in both the t_{2g}- and e_g-orbitals, as in the nomenclature of ref. 5 (cf. the footnote in the preceding paper). For the t^3_{2g} configuration $\lambda = \zeta/3$.

[1] Owen, Cooke, Lazenby, McKim, and Wolf, *Proc. Roy. Soc.*, 1959, *A*, **250**, 97.
[2] Cf. Liddiard, *Reports Progr. Phys.*, 1954, **17**, 201.
[3] Penney and Schlapp, *Phys. Rev.*, 1932, **42**, 666.
[4] Figgis, *Trans. Faraday Soc.*, 1960, **56**, 1553.
[5] Owen, *Proc. Roy. Soc.*, 1955, *A*, **227**, 183.
[6] Condon and Shortley, " Theory of Atomic Spectra," Cambridge University Press, 1935.

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ground level with an admixture of the $^2T_2$ term which also arises from the t^3_{2g} configuration. The magnetic behaviour of t^3_{2g} in intermediate coupling has been discussed; the g values for the $^4A_2$ term and the magnetic moment as a function of the parameter kT/ζ have been given.[7,8] For spin–orbit coupling constants large enough to require the intermediate coupling treatment, the effect of temperatures of 300° K or below is not important, and in Fig. 1 we have given μ_{eff} for the $^4A_2$ term at zero temperature, as a fraction of the spin-only moment ($\mu_{s.o.}$) in the Russell–Saunders coupling limit. The parameter against which μ_{eff} is plotted is $\eta = \zeta/(3B + C)$, which is a measure of the degree of $j \cdot j$ coupling.

Of course, in the intermediate coupling scheme, the $^4A_2$ term is still subject to interaction with the higher ligand field $^4T_1$ term. A full treatment of the problem would require that the behaviour of the $^4A_2$ term be studied under simultaneous perturbation by interaction with the $^4T_1$ term and the influence of $j \cdot j$ coupling. However, for the ions of importance to the present work, the degree of $j \cdot j$ coupling is small and we have assumed that the

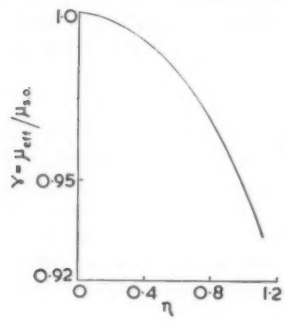


FIG. 1. *The magnetic moment of the t^3_{2g}-configuration in the intermediate coupling scheme.*

two interactions affect the moment of the term independently. Thus, if $\mu_{i.c.}$ is written for the moment of t^3_{2g} set in the intermediate coupling scheme, then

$$\begin{aligned} \mu_{eff} &= \mu_{i.c.}(1 - 4\lambda''/10Dq) \\ &= \gamma\mu_{s.o.}(1 - 4\lambda''/10Dq). \end{aligned} \quad \ldots\ldots\ldots \quad (3)$$

The influence of asymmetry in the ligand field on the temperature-variation of the moment of the $^4A_2$ term is expected [4] to increase as ζ^2 and to decrease as $[10Dq]^2$. Since ζ' is very large in the complexes studied here it would be possible for a large asymmetry in the ligand field to affect appreciably the moment at temperatures as high as 80° K, in spite of the fact that $10Dq$ also is large. However, the complexes have six equivalent ligand atoms surrounding the central metal ion, and it is not expected that the asymmetry will be large. Thus it is unlikely that this effect could be entirely responsible for the great variation of the moment with temperature which occurs for the rhenium compounds. This is especially true when it is considered that such variations are not observed for the complexes of osmium and iridium where ζ' is greater than for rhenium. We have therefore not taken this effect into account. We have interpreted the variation of the moment of rhenium compounds with temperature and between solid and solution as reflecting magnetic interactions.

In order to compare our results with the theory outlined above, it is necessary to know the values of the parameters of spin–orbit coupling and interelectronic repulsion within the ions of the complexes. Such values are not available from direct measurement, nor are they available for the free ions from observation of the spectra, except for Mo^{3+}. Consequently, we have estimated the free-ion values of the parameters from a knowledge of those of the first-row and a few second-row transition-element ions, assuming that the

[7] Goodman, Fred, Moffitt, and Weinstock, *Mol. Phys.*, 1959, **2**, 109.
[8] Kamimura, Koide, Sekiyama, and Sugano, *J. Phys. Soc. Japan*, 1960, **15**, 1264.

trends shown between the first and the second row, and between ions of increasing charge, are maintained. The estimates so obtained are set out in Table 1. The estimation

TABLE 1. *Estimated values of the spin–orbit coupling and interelectronic repulsion parameters, and the ratio* $\eta = \zeta/(3B + C)$*, for the ions studied (free-ion values).*

	Ion	ζ (cm.$^{-1}$)	$3B + C$ ($3F_2 + 20F_4$) (cm.$^{-1}$)	η		Ion	ζ (cm.$^{-1}$)	$3B + C$ ($3F_2 + 20F_4$) (cm.$^{-1}$)	η
$3d^3$	Cr^{3+}	275 *	6200	0·04	$5d^3$	Re^{4+}	3300	3700	0·9
$4d^3$	Mo^{3+}	840 *	4300	0·2		Os^{5+}	4500	4200	1·1
						Ir^{6+}	6000	4700	1·3

B and C are Racah parameters of interelectronic repulsion; F_2 and F_4 are Condon–Shortley parameters.

* This value was obtained from the spectrum of the ion.

procedure cannot be considered to be more reliable than about $\pm 20\%$ for each of the parameters. However, it is probable that the same type of error is present in the estimation of each of the parameters, so the ratio $\eta = \zeta/(3B + C)$ will also be reliable to about $\pm 20\%$. A detailed account of the estimation of these parameters is to be published by Dr. T. M. Dunn. In order to compare the behaviour of the complexed ion, rather than the free ion, we have assumed that, in the complexed, the ratio of the spin–orbit coupling and the interelectronic repulsion parameters is unchanged, while the spin–orbit coupling parameter for use in $(1 - 4\lambda''/10Dq)$ is reduced from the free-ion value by the factor $\alpha^2 k$. On this approximation, η is independent of the ligand environment of the ion. Here α^2 allows for the delocalisation from the e_g orbitals connected with the $^4T_1$ term, while k allows for delocalisation from the t_{2g} orbitals. Thus $\lambda'' = \alpha^2 k\zeta/3$.

Results.—The results of the measurements of the magnetic susceptibility of twenty-one complexes of Cr^{III}, Mo^{III}, Re^{IV}, Os^{V}, and Ir^{VI} between 80° and 300° K, are set out in Table 2. μ_{eff} is plotted as a function of temperature in Figures 2—7. The results for only two of the complexes of chromium are given diagrammatically, because those for the other complexes are very similar. The results are summarised in Table 3. The mesasurements made in aqueous solution are included in Table 4.

TABLE 2. *Magnetic susceptibilities of the compounds studied. Temperatures in degrees* K, *susceptibilities in* 10^{-6} c.g.s./mole.

Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal
$K_3Cr(CN)_6$		$Cr(acac)_3$		$K_3Cr(CNS)_6,4H_2O$		Cr en$_3$Cl$_3$,3H$_2$O		Cr en$_3$Br$_3$,3H$_2$O		Cr en$_3$I$_3$,H$_2$O	
294·7°	6296	295·2°	6268	295·2°	6046	302·5°	6003	300·8°	6151	301·2°	6063
269·6	6923	270·3	6827	269·1	6634	278·9	6491	276·3	6673	277·2	6576
245·0	7536	245·5	7466	245·9	7275	253·2	7106	250·2	7334	251·1	7217
221·7	8331	222·0	8230	221·7	8035	229·2	7812	224·6	8119	226·1	7984
197·9	9287	198·1	9158	197·9	8949	204·4	8719	200·3	9103	201·0	8924
174·7	10,533	174·9	10,339	175·0	10,141	179·0	9915	174·7	10,390	173·8	10,270
151·4	12,083	152·0	11,819	151·7	11,611	151·1	11,710	143·5	12,630	147·4	12,080
129·2	14,183	130·0	13,789	129·4	13,601	124·7	14,160	124·7	14,440	123·8	14,330
105·6	17,190	106·5	16,630	105·4	16,880	106·2	16,590	103·6	17,410	103·6	17,150
81·2	22,350	82·1	21,470	82·1	21,110	85·0	20,800	84·6	21,340	79·7	22,140

Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal
K_3MoCl_6		$K_3Mo(CNS)_6,4H_2O$		K_2ReF_6		Cs_2ReF_6		K_2ReCl_6		Cs_2ReCl_6	
296·3°	6021	297·5°	5971	293·8°	4654	259·3°	4640	292·0°	4490	295·3°	4712
271·7	6537	273·0	6495	269·4	4843	270·6	5063	269·5	4770	271·0	5064
247·3	7144	248·6	7101	259·8	5075	246·0	5462	247·3	5074	246·6	5455
223·4	7880	222·4	7883	232·9	5561	222·3	6000	225·1	5450	223·0	5954
199·7	8762	193·1	9059	209·0	6147	198·5	6619	202·3	5903	199·2	6538
176·6	9847	168·8	10,321	191·7	6601	175·2	7412	178·5	6399	176·0	7210
152·7	11,265	143·0	12,231	168·5	7261	152·0	8378	155·6	6985	152·7	8045
131·3	12,990	117·7	14,820	151·0	7912	129·5	9619	132·9	7703	129·5	9170
109·3	15,370	104·6	16,610	127·4	8776	104·4	11,450	109·9	8563	104·0	10,730
86·2	18,960	79·8	21,500	116·0	9946	80·9	13,850	86·6	9560	80·0	12,870

XUM

TABLE 2. (*Continued.*)

Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal
$(PyH)_2ReCl_6$		$(QH)_2ReCl_6$		$(TH)_2ReCl_6$		Cs_2ReBr_6		K_2ReI_6		Cs_2ReI_6	
297·4°	5339	294·6°	5282	303·7°	4989	304·3°	4605	292·2°	4661	296·5°	4323
271·3	5803	271·1	5691	279·0	5393	279·8	4918	269·6	4922	270·6	4535
246·0	6330	246·8	6159	253·6	5830	254·4	5247	247·3	5262	245·6	4811
222·2	6952	220·7	6840	229·9	6346	232·8	5628	225·1	5665	221·0	5162
197·5	7759	192·1	7767	206·2	6941	206·0	6135	202·3	6117	196·3	5558
174·0	8703	169·0	8739	182·5	7703	183·3	6682	178·7	6624	172·1	5992
151·1	9987	146·0	10,030	160·0	8559	160·9	7293	155·5	7223	149·4	6454
130·2	11,500	118·5	12,140	138·1	9713	138·4	8076	132·7	7911	136·3	6702
106·7	13,830	104·5	13,724	119·7	10,840	121·5	8756	107·8	8800	128·4	6943
79·4	17,960	80·3	17,390	104·0	12,120	104·9	9525	86·6	9654	104·2	7635
				79·8	14,710	79·8	10,940			80·0	8465

Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal	Temp.	Metal
$KOsF_6$		$KOsF_6$		$CsOsF_6$		$CsOsF_6$		IrF_6		IrF_6	
295·2°	4613	182·7°	7401	293·7°	4393	190·0°	6798	293·6°	3725	172·6°	5784
273·2	4945	167·4	8380	269·7	4700	169·0	7565	265·1	3835	152·6	6442
252·7	5364	151·5	8891	253·0	5137	155·5	8251	243·6	4233	132·7	7182
219·3	6200	137·5	10,180	244·0	5345	133·7	9578	220·9	4647	112·1	8286
196·7	6892	115·0	11,430	224·7	5780	118·0	10,760	196·8	5165	90·1	9855
				205·7	6308						

TABLE 3. *Summary of magnetic moments at* 300°K *and the Weiss constants of the complexes studied.*

Compound	μ_{eff} (300°K)	θ	Compound	μ_{eff} (300°K)	θ	Compound	μ_{eff} (300°K)	θ
$K_3Cr(CN)_6$	3·87	1°	$K_3Mo(CNS)_6.4H_2O$	3·79	3°	$(TH)_2ReCl_6$ [e] ...	3·50	35°
$Cr(acac)_3$ [a]	3·86	7	K_2ReF_6	3·30	40	Cs_2ReBr_6	3·36	80
$K_3Cr(CNS)_6.4H_2O$	3·79	2	Cs_2ReF_6	3·32	24	K_2ReI_6	3·32	100
$Cr\,en_3Cl_3.3H_2O$ [b]	3·83	4	K_2ReCl_6	3·25	88	Cs_2ReI_6	3·22	135
$Cr\,en_3Br_3.3H_2O$...	3·82	4	Cs_2ReCl_6	3·35	45	$KOsF_6$	3·34	0
$Cr\,en_3I_3.H_2O$.....	3·84	5	$(PyH)_2ReCl_6$ [c]	3·58	14	$CsOsF_6$	3·23	0
K_3MoCl_6	3·79	11	$(QH)_2ReCl_6$ [d]	3·54	13	IrF_6	(2·90) [f]	30

[a] acac = acetylacetone. [b] en = ethylenediamine. [c] PyH = pyridinium. [d] QH = quinolinium. [e] TH = *p*-toluidinium. [f] There is scatter in the experimental data for this compound at high temperatures, and the moment cannot be given accurately at 300° K.

TABLE 4. *Magnetic susceptibilities of compounds of molybdenum and rhenium in solution.*

Compound	Solvent	Concn. (M)	Temp. (K)	$10^6\chi_A$	μ_{eff}
K_3MoCl_6	4N-HCl	0·080	293°	5906	3·74
K_2ReF_6	H_2O	0·040	293	4979	3·43
K_2ReCl_6	4N-HCl	0·050	293	5382	3·55
K_2ReBr_6	8N-HBr	0·040	295	5346	3·56
K_2ReI_6	9N-HI	0·050	295	5313	3·55

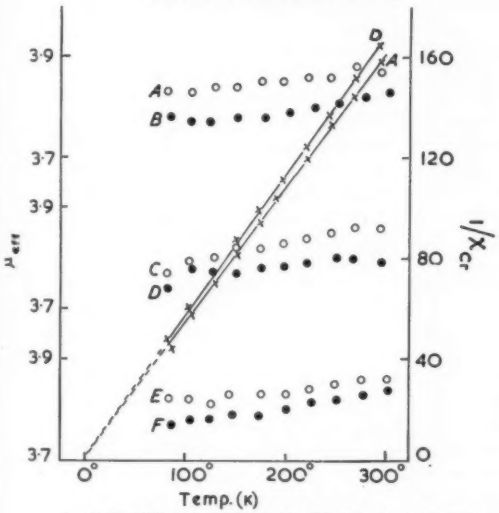
DISCUSSION

Chromium.—With $\lambda = 91$ cm.$^{-1}$ and $10Dq \approx 20{,}000$ cm.$^{-1}$, the moments of Cr^{III} complexes are reduced below the spin-only value through operation of eqn. (2) by only some 2%, or less if λ'' is lower than λ. Such a reduction is not far outside the experimental error of the measurements. The moments of the chromium complexes studied fall in the range 3·74—3·87 B.M., which is centered around the 3·81 B.M. expected. The spin–orbit coupling constant is so small that application of the intermediate coupling results have no effect on the moment which is predicted. In agreement with the theory the moments vary very little with temperature.

Molybdenum.—For tervalent molybdenum, with $\lambda = 280$ cm.$^{-1}$ and $10Dq \approx 20{,}000$ cm.$^{-1}$, applcation of eqn. (2) leads to a moment as much as 5·6% below the spin-only value. Although the spin-orbit coupling constant is a good deal larger than for chromium, effects of intermediate

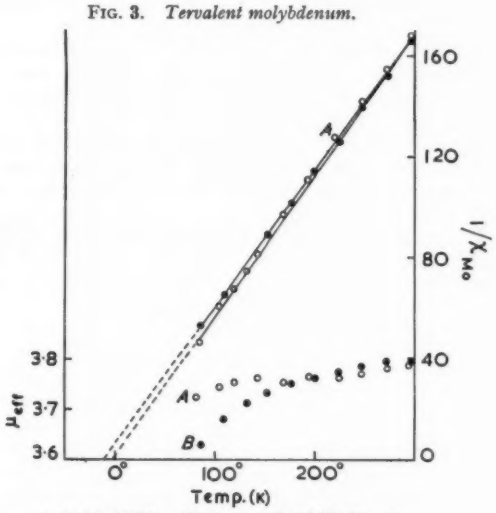
FIGS. 2—7. *Plots of μ_{eff} and $1/\chi_{Metal}$ against temperature.*

FIG. 2. *Tervalent chromium.*



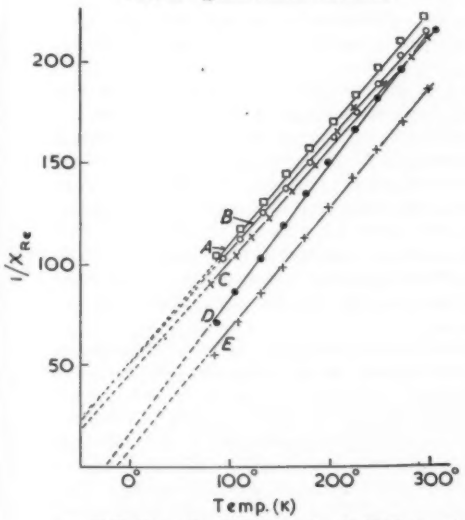
A, $K_3Cr(CN)_6$; *B*, $Cr(en)_3Cl_3,3H_2O$; *C*, $Cr(acac)_3$; *D*, $K_3Cr(CNS)_6,4H_2O$; *E*, $Cr(en)_3I_3,H_2O$; *F*, $Cr(en)_3Br_3,3H_2O$. × refers to $1/\chi_{Cr}$ and the right-hand ordinate.

FIG. 3. *Tervalent molybdenum.*



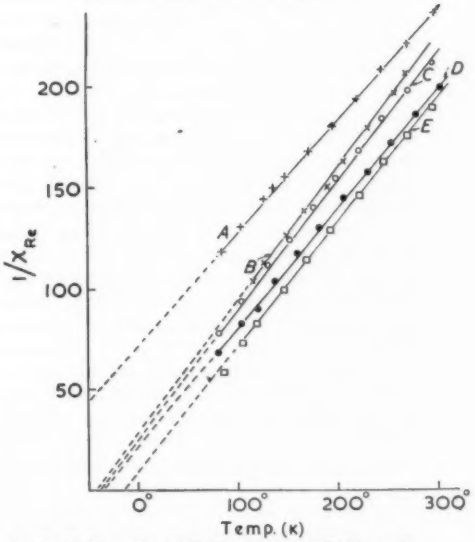
A, $K_3Mo(CNS)_6,4H_2O$ ○; *B*, K_3MoCl_6, ●.

FIG. 4. *Quadrivalent rhenium.*



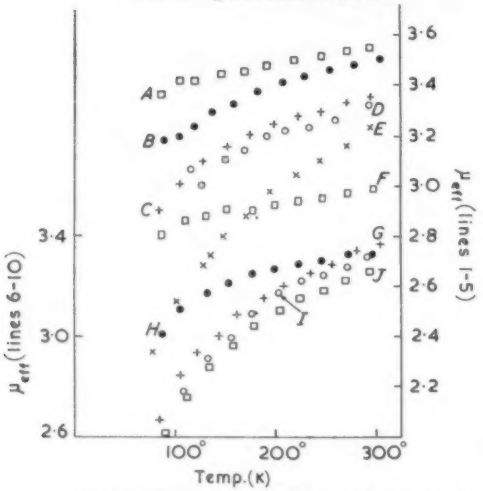
A, K_2ReCl_6; *B*, K_2ReI_6; *C*, Cs_2ReBr_6; *D*, Cs_2ReF_6; *E*, $(PyH)_2ReCl_6$.

FIG. 5. *Quadrivalent rhenium.*



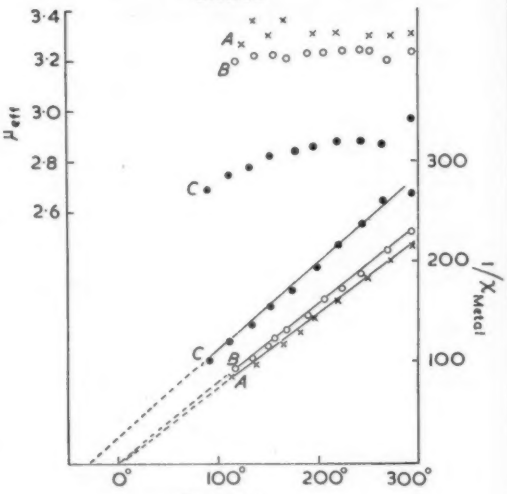
A, Cs_2ReI_6; *B*, K_2ReF_6; *C*, Cs_2ReCl_6; *D*, $(TH)_2ReCl_6$; *E*, $(QH)_2ReCl_6$.

FIG. 6. *Quadrivalent rhenium.*



A, $(QH)_2ReCl_6$; *B*, $(TH)_2ReCl_6$; *C*, Cs_2ReCl_6; *D*, K_2ReF_6; *E*, Cs_2ReI_6; *F*, $(PyH)_2ReCl_6$; *G*, Cs_2ReF_6; *H*, Cs_2ReBr_6; *I*, K_2ReI_6; *J*, K_2ReCl_6.

FIG. 7. *Quinquevalent osmium and sexivalent iridium.*



A, $KOsF_6$; *B*, $CsOsF_6$; *C*, IrF_6.

coupling are negligible: for $\eta = 0{\cdot}2$ the moment is reduced by only 0·2%. The moment observed for the hexachloromolybdate(III) ion varies appreciably with temperature: $\theta = 11°$. Rather than correct the moment with the aid of eqn. (1), we accepted the value of μ_{eff} for this ion in solution. The two complexes of molybdenum(III) studied then yield moments about 3% below the spin-only value. The reduction in moment is too small to allow an accurate evaluation of λ'', but it seems that it is about $0{\cdot}5\,\lambda$, *i.e.*, $\alpha^2 k \approx 0{\cdot}5$. A 50% reduction in the effective spin–orbit coupling parameter by delocalisation effects is not unreasonable for the hexachloro- and hexathiocyanato-molybdate(III) ions.

Rhenium.—For quadrivalent rhenium the effect of the intermediate coupling scheme becomes of some importance. For $\eta = 0{\cdot}9$ the moment is reduced by the factor $\gamma = 0{\cdot}96$. Under the influence of eqn. (2), with $\lambda = 1100$ cm.$^{-1}$ and $10Dq \approx 27{,}000$ cm.$^{-1}$, the moment could be reduced by 16%. The magnetic moment exhibited by the rhenium atom in the hexahalogenorhenate(IV) complexes studied here is not known with the certainty which is desirable. The moments vary with temperature in a manner which suggests magnetic exchange interactions are present. However, even though Weiss constants as high as 135° have been found, our measurements give no indication of the existence of a Curie temperature. Consequently, it seems that the substances cannot be regarded as well-behaved antiferromagnetics. For this reason we have not attempted to use moments calculated on the basis of eqn. (1) for comparison with the theory.

In order to obtain data not subject to uncertainty from magnetic exchange effects, we studied hexahalogenorhenates(IV) with large organic cations, in the hope that these would provide adequate magnetic dilution. While the magnetic exchange appears to be less in such compounds, it is by no means absent. The magnetic exchange in these systems will depend critically on (*a*) the tendency of the electron to be transferred to the ligand and (*b*) the halogen–halogen separation between ions in the solid. We therefore expect that the interaction may vary radically on changing the nature of both the co-ordinating anion and the cation. This effect is illustrated by the value of θ for the hexachlororhenate ion when the cation is varied. The value of θ is low for the pyridinium and quinolinium salts, but relatively high for the potassium and *p*-toluidinium salts. We have found the latter pair of salts to be isomorphous; the former pair have different structures. The compounds K_2ReF_6, K_2ReCl_6, and K_2ReBr_6

are reported to be isomorphous with K_2PtCl_6 and cubic,[9] whilst K_2ReI_6 is reported to be orthorhombic,[10] and in this series it appears that the antiferromagnetic interaction increases in the order $F < Cl < Br < I$. We therefore used the results obtained on the ions in solution, though the accuracy is not high, as the solubilities of the ions are low, and measurement over reasonable temperature range is not possible.

The solution measurements lead to the conclusion that $\mu_{eff} = 0{\cdot}915\,\mu_{s.o.}$. If η is taken to be the estimated 0·9, the delocalisation factor α^2k has to be 0·3, a rather improbably small value. However, if ζ is reduced to 2600 cm.$^{-1}$, which is within the range of the accuracy we have allowed for, the estimated value of η is reduced to 0·7, $\gamma = 0{\cdot}975$, and α^2k becomes 0·5. Such a value of the delocalisation parameter is reasonable. As comparison between theory and experiment is only approximate we do not consider the results for the individual compounds of each ion. We are attempting to obtain more results for the ions in order to be able to correlate the delocalisation factor with the halogen ligand atom.

Osmium.—Our studies on quinquevalent osmium include two hexafluoro-complexes. Their moments do not vary with temperature. Since they involve the same hexafluoro-osmate(v) ions with rather similar cations, and the moments do not differ much, we will compare the mean of the two values (3·29 B.M. = $0{\cdot}85\,\mu_{s.o.}$) with theory. The estimated value of η (1·1) leads to $\gamma = 0{\cdot}91$. With $\lambda = 1500$ cm.$^{-1}$, a delocalisation factor of 0·4 is required to account for the rest of the reduction in moment. A small reduction in ζ enables a larger value of α^2k to be employed, and that may be considered more suitable for a fluoro-complex.

Iridium.—We have results only for iridium hexafluoride. Its moment varies with temperature ($\theta = 30°$), and we could not make measurements on it in a more magnetically dilute form. Since the use of eqn. (2) in connection with the compounds of rhenium leads to moments higher than those obtained from the measurements on solutions, we have hesitated to apply it to the IrF_6 result. μ_{eff} for the compound is ~2·90 B.M. at 300° K (there is a little uncertainty about the results at high temperature); when corrected by the use of eqn. (1) this becomes 3·05 B.M. With η estimated as 1·3 for Ir^{6+}, γ is 0·91. If α^2k is taken to be 0·5, λ'' is 1000 cm.$^{-1}$, and if $10Dq$ is estimated to be 30,000 cm.$^{-1}$ this leads to a calculated moment of 3·05 B.M. In view of the uncertainty in the moment and the approximations involved in the theory, for which each of $3B + C$ and $10Dq$ are available only as estimates, it does not seem worthwhile pursuing the details of this agreement.

From the preceding discussion it may be concluded that the magnetic properties of the t^3_{2g} compounds studied are in accord with the theory for the configuration if reasonable values of the parameters which govern the theory are employed. However, the results are too limited, and their significance is reduced too much by magnetic exchange, for comparison between theory and experiment to be more than semiquantitative. Since it is unlikely that further complexes of quinquevalent osmium or sexivalent iridium will become available, it appears that future work on elucidating the magnetic behaviour of the configuration will depend on obtaining hexahalogenorhenates(IV), or other quadrivalent rhenium complexes, in higher magnetic dilution. The main feature of the application of the intermediate coupling scheme is that it allows a considerable amount of electron delocalisation to be assumed; without this scheme, the use of eqn. (2) would indicate that no delocalisation takes place.

Experimental.—The compounds employed were prepared and analysed by standard methods. The authors are indebted to Dr. R. D. Peacock for the loan of the fluoride complexes and to Dr. A. Earnshaw for the measurement of the magnetic susceptibilities of these. The accuracy of the measurement of the absolute magnetic susceptibilities was 2—3%, that of the relative susceptibility of the same compound at different temperatures was about 0·5%,[11] except that for iridium hexafluoride, which is volatile, the results at about room temperature show scatter.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER STREET,
LONDON, W.C.1.

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603. *The Scope and Mechanism of Carbohydrate Osotriazole Formation. Part VI.*[1] *The Apparent Dissociation Constant of Triazole Carboxylic Acids.*

By H. El Khadem.

It has been shown[1,2] that *o*-halogeno-phenylosotriazoles and -benzoic acids undergo dehalogenation by copper powder, it being suggested that the triazole ring acted as an electron-attracting group, rendering the *o*-halogen atom more reactive. To study the influence of substituents on the strength of triazolecarboxylic acids, the apparent dissociation constants of 2-*m*- and 2-*p*-carboxyphenyl-1,2,3-triazole and of some 2-arylphenyl-1,2,3-triazole-4-carboxylic acids have been determined and compared with those of substituted benzoic acids. The dissociation constants of a few triazolecarboxylic acids were determined previously,[3] but these did not include the 2-phenyl derivatives. Owing to the sparing solubility of the acids in water, their dissociation constants were determined in the solvent system 4 : 1 w/w Methylcellosolve–water.[4] The results are shown in the Table.

Acid	p*K*
2-*m*-Carboxyphenyl-1,2,3-triazole [1]	6·12
Glucose *m*-carboxyphenylosotriazole [2]	6·22
2-*p*-Carboxyphenyl-1,2,3-triazole [2]	6·24
Glucose *p*-carboxyphenylosotriazole [2]	6·31
2-Phenyl-1,2,3-triazole-4-carboxylic [5]	4·98
2-*m*-Chlorophenyl-1,2,3-triazole-4-carboxylic [1]	4·81
2-*p*-Chlorophenyl-1,2,3-triazole-4-carboxylic [1]	4·84
2-*m*-Bromophenyl-1,2,3-triazole-4-carboxylic [6]	4·83
2-*p*-Bromophenyl-1,2,3-triazole-4-carboxylic [5]	4·81
2-*m*-Iodophenyl-1,2,3-triazole-4-carboxylic [1]	4·84
2-*p*-Iodophenyl-1,2,3-triazole-4-carboxylic [1]	4·81
2-*m*-Methoxyphenyl-1,2,3-triazole-4-carboxylic [2]	4·98
2-*p*-Methoxyphenyl-1,2,3-triazole-4-carboxylic [2]	5·09
2-*p*-Nitrophenyl-1,2,3-triazole-4-carboxylic [7]	4·54
2-*m*-Carboxyphenyl-1,2,3-triazole-4-carboxylic [6]	4·93, 6·54
2-*p*-Carboxyphenyl-1,2,3-triazole-4-carboxylic [5]	4·72, 6·47

Experimental.—Preparation of the acids is described in the literature cited.

The apparent dissociation constants have been determined by titrating ~0·037M-solutions of the acids in 4 : 1 w/w Methylcellosolve–water with aqueous 0·1N-tetramethylammonium hydroxide. The apparent pH measured with a glass–calomel electrode system at half-neutralisation was recorded as p*K*. The results given are the mean of two determinations. The standard error of a single determination is 0·07 p*K* unit (95% level of significance).

Discussion.—From the measurements we find that 2-phenyltriazoles having a carboxy-group attached to the benzene ring have p*K* 6·12—6·31 and are thus stronger acids than benzoic acid [8] (p*K* 6·63). Thus, in the 2-phenyltriazole system there is an electron-shift towards the triazole ring, in harmony with our previous view.

Further, the p*K* values of triazole-3-carboxylic acids are 4·52—5·09 and are thus much stronger acids than the carboxyphenyl derivatives. It follows that the triazole ring is a much stronger electron-attracting group than the benzene ring.

A plot of p*K* against σ (determined from the equation $pK = 4{\cdot}98 - 0{\cdot}437\sigma$) is an approximate straight line. Comparison with the results for benzoic acid [8] shows similar

[1] Part V, *J.*, 1961, 2957.
[2] El Khadem, El-Shafei, and Mohammed, *J.*, 1960, 3993.
[3] Benson and Savell, *Chem. Rev.*, 1950, **46**, 1.
[4] Simon, *Helv. Chim. Acta*, 1958, **41**, 1835.
[5] El Khadem and El-Shafei, *J.*, 1958, 3117.
[6] El Khadem and El-Shafei, *J.*, 1959, 1655.
[7] Bischop, *Science*, 1953, **117**, 715.
[8] Simon, Lyssy, Mörikofer, and Heilbronner, "Zusammenstellung von scheinbaren Dissoziationskonstanten im Lösungsmittelsystem Methylcellosolve/Wasser," Juris-Verlag, Zürich, 1959, p. 5.

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effects for substituents. The value of ρ in Hammett's equation,[9] determined from the slope of the plot for the triazole acids by the method of least squares, is only 0·45 (cf. 1·665 for substituted benzoic acids). This we attribute to the fact that the substituents here are separated from the carboxy-group by two ring systems, so that they will influence it only to a limited degree.

The author thanks Dr. W. Simon and Dr. P. F. Sommer for the dissociation-constant measurements.

CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE, ALEXANDRIA UNIVERSITY,
ALEXANDRIA, EGYPT, U.A.R. [*Received, December 29th*, 1960.]

[9] Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 96.

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604. *Trisethylenediaminenickel*(II) *Thiosulphate as a Calibrant for Susceptibility Measurements by the Gouy Method.*

By N. F. CURTIS.

THE use of mercury tetrathiocyanatocobaltate, $HgCo(CNS)_4$, as a calibrant for magnetic susceptibility measurements by the Gouy method has been described by Nyholm and Figgis.[1] However, the susceptibility of this compound has been found to be too large for convenience in some applications. Thus, lateral displacement of the Gouy tube filled with this material, caused by field inhomogeneity, is troublesome for tubes of large diameter, or with the high field strengths which are desirable for measurements on compounds of low susceptibility. This is particularly serious in the narrow space usually available when temperature-controlling apparatus is fitted within the pole gap.

Trisethylenediaminenickel(II) thiosulphate has been found to be a satisfactory alternative in these circumstances, the force exerted by a magnetic field on a tube filled with this compound being approximately one-third of that exerted when the tube is filled with the mercury compound, and the lateral displacement effects are very much smaller. This complex, Ni $en_3S_2O_3$, is readily prepared, in a form which packs readily and uniformly in a Gouy tube and is unaffected by exposure to the atmosphere. In these respects it is much superior to crushed copper sulphate pentahydrate, which is often used as a calibrant of low susceptibility.

The magnetic susceptibility of five samples of Ni $en_3S_2O_3$, prepared under a variety of conditions, was determined at 25°, with three preparations of $HgCo(CNS)_4$ for calibration. In each case, the results quoted are the average of six measurements.

(a) *Calibration of Gouy tube.* [10^3,$W/\Delta w$. χ_g for $HgCo(CNS)_4$] 5·062 (±0·5%), 5·006 (±0·5%), 5·067 (±0·6%). Average 5·044 (±0·2%).

(b) *Susceptibility of* Ni $en_3S_2O_3$ $10^6\chi_g$. 10·76 (±0·3%), 10·72 (±0·5%), 10·83 (±0·7%), 10·81 (±0·6%), 10·99 (±0·9%). Average 10·82 (±0·4%).

The first sample, the preparation of which is described, gave particularly uniform results and was used for the measurements described in (c) and (d).

(c) *Temperature variation of susceptibility.* The susceptibility was measured at 1°, 25°, and 52°, with the same tube-full of Ni $en_3S_2O_3$. The average of four such series of measurements shows that, in the range studied, the compound obeys the Curie–Weiss law $\chi_g \propto [T - (43 \pm 5)]^{-1}$, T being in degrees absolute.

(d) *Variation of sample length.* To check the uniformity with which the compound packed in the sample tube, the susceptibility was measured with the Gouy tube filled to 8 cm., instead of the 12 cm. used for all other measurements. The determined value,

[1] Nyholm and Figgis, *J.*, 1958, 4190.

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$\chi_g = 10{\cdot}82\ (\pm 0{\cdot}4\%) \times 10^{-6}$, agrees well with the value calculated from the measurements with 12 cm. sample length, for the same preparations of $Ni\,en_3S_2O_3$ and $HgCo(CNS)_4$, namely, $10{\cdot}79\ (\pm 0{\cdot}7\%) \times 10^{-6}$.

The gram-susceptibility at 25° is taken to be $10{\cdot}82\ (\pm 10) \times 10^{-6}$ (including the 0·5% uncertainty in the value of the susceptibility of the calibrant [1]).

Experimental.—Measurements were performed with a flat-bottomed Pyrex tube of 3·3 mm. diameter, suspended from the pan of an aperiodic semimicro-balance. The magnetic field was provided by an " Alcomax " permanent magnet of field strength about 7500 gauss, with pole-pieces 1 in. in diameter, and $\frac{3}{4}$ in. apart. During measurements the position of the Gouy tube in the magnetic field was maintained within 0·5 mm. by using the overlapping optical and rider ranges (both of 10 mg.), although variation in the force exerted by the magnetic field on the sample tube was negligible over the full optical range. The Gouy tube was surrounded by a double-walled glass jacket through which water from a thermostat bath was pumped. The temperature of the specimen was measured by means of a thermometer in this water jacket, preliminary measurements having shown that this gave a reliable indication of the temperature of the specimen at thermal equilibrium. Before the ice-water was circulated for the low-temperature measurements, the air was displaced from around the Gouy tube by means of a stream of dry nitrogen, to prevent condensation on the tube.

The Gouy tube was filled with the appropriate compound, which was compacted by repeatedly allowing the tube to fall from a height of about 2 in. on to wood. There was no systematic variation in results between measurements with the tube contents added in small portions, with compaction between additions (as described by Nyholm and Figgis), and those where the contents were compacted after the tube had been filled. The sample weight with $Ni\,en_3S_2O_3$ was about 0·8 g., and the force exerted by the magnetic field 17 mg. The figures for $HgCo(CNS)_4$ were 1·6 g. and 50 mg. respectively.

Preparation. To a vigorously boiling solution of " AnalaR " nickel nitrate hexahydrate (2 g.) and ethylenediamine hydrate (2 ml.) in water (50 ml.) was added a boiling solution of sodium thiosulphate pentahydrate (2 g.) in water (20 ml.). The whole was boiled for a minute and stirred vigorously as it cooled. The mauve crystals were filtered off from the cold solution, washed with cold water and then ethanol, and dried at 100° (Found: Ni, 16·7; C, 21·0; H, 6·9; N, 23·9. Calc. for $C_6H_{24}N_6NiO_3S_2$: Ni, 16·7; C, 20·5; H, 6·8; N, 23·9%). Before use, the crystals were vigorously agitated, to break up any crystal aggregates.

A sample (0·6 g.) showed no loss in weight when heated for several days at 110°, and this sample then showed no change in weight when exposed to the atmosphere for several days.

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CHEMISTRY DEPARTMENT,
VICTORIA UNIVERSITY OF WELLINGTON, NEW ZEALAND. [*Received, December* 30*th*, 1960.]

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605. *Tris*-(2-*hydroxyethyl*) *Isocyanurate.*

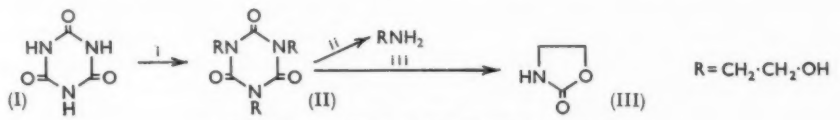
By A. A. SAYIGH and H. ULRICH.

CYANURIC ACID (I) has seldom been used as a nucleophilic reagent in reactions to yield isocyanurates containing functional groups. Recently,[1] however, and concurrently with our work a number of these compounds were reported. Thus tris-(2-hydroxyethyl) isocyanurate (II) was recently reported [1] to have been prepared from cyanuric acid and ethylene oxide. Previously, using the same reagents, we obtained only a mixture of products from which (II) could not be isolated.

The synthesis of the isocyanurate (II) in 83% yield by reaction of cyanuric acid and 2-chloroethanol in alkaline medium has been found to be convenient and reproducible,

[1] (*a*) U.S.S.R. Patent 118,042/1959 (*Chem. Abs.*, 1960, **53**, 21,673); (*b*) Frazer, Little, and Lloyd, *J. Org. Chem.*, 1960, **25**, 1944.

whereas previously known general methods [2] for the preparation of trialkyl isocyanurates could not be adapted to the synthesis of the hydroxyethyl compound (II).



i, RCl/HO⁻. ii, HO⁻. iii, Hot dimethylformamide.

Aqueous alkaline hydrolysis gave ethanolamine, and heating in dimethylformamide at 150—155° converted (II) into oxazolidone (III). The latter was identified by its infrared spectrum which was identical with that of a sample prepared according to Fränkel and Cornelius's method.[3]

Experimental.—Tris-(2-hydroxyethyl) isocyanurate (II). A suspension of cyanuric acid (65 g.) in water (748 ml.) containing sodium hydroxide (14·4 g.) was stirred vigorously and heated to 90—95°; a cold solution of 2-chloroethanol (290 g.) and sodium hydroxide (80 g.) in water (390 g.) was added dropwise during 6—8 hr., the temperature being kept at 95°. The resulting clear solution (pH 8·6—9·1) was set aside overnight, and then concentrated *in vacuo* (steam-bath). The resulting oil and solid were extracted with boiling isopropyl alcohol or dioxan (5 × 100 ml.); the combined extracts were filtered hot, cooled to 8°, and filtered again to give the solid product. Concentration (to *ca.* 75 ml.) of the mother liquor *in vacuo* and cooling overnight to 8° gave a precipitate which was collected. The combined solids were washed with cold isopropyl alcohol (50 ml.) and dried. The product (II) (109 g.; 83% yield) had m. p. 135—136° (lit.,[1a] 134—136°) (Found: C, 41·7; H, 5·9; N, 16·2. Calc. for $C_9H_{15}N_3O_6$: C, 41·4; H, 5·8; N, 16·1). Its infrared spectrum in potassium bromide is identical with that of an authentic sample: * 2·95s, 3·07m, 3·35w, 3·45w, 5·95vs, 6·85vs, 7·35m, 7·55m, 7·85w, 7·95w, 8·68w, 9·47m, 9·65m, 10·1w, 11·05w, 11·25w, 11·65w, 13·05m, 13·41w μ.

Oxazolidone (III). The isocyanurate (II) (10 g.) was heated in dimethylformamide (100 ml.) at 150—155° for 6 hr. The infrared spectrum of the solution was identical with that of a dimethylformamide solution containing the oxazolidone (III), prepared according to Fränkel and Cornelius.[3]

We thank Mr. F. J. Geremia for experimental assistance.

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[*Received, January 4th*, 1961.

* Kindly supplied by Allied Chemical Corporation, Nitrogen Division, Hopewell, Virginia, U.S.A.

[2] Biilmann and Bjerrum, *Ber.*, 1917, **50**, 503; Bortnick, Luskin, Hurwitz, and Rytina, *J. Amer. Chem. Soc.*, 1956, **78**, 4358; U.S.P. 2,536,849/1959.
[3] Fränkel and Cornelius, *Ber.*, 1918, **51**, 1654.

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606. *The Preparation of* o-(4-*Phenylbuta*-1,3-*dienyl*)*phenylboronic Anhydride.*

By P. M. MAITLIS.

THE seven-membered fully conjugated borepin ring is of theoretical interest as it should be aromatic. Our attempts to synthesise a derivative containing it from the boronic anhydride (II) have, however, failed.

1-*o*-Bromophenyl-4-phenyl-1,3-butadiene (I) was prepared in 33% yield from *o*-bromophenylacetic acid and cinnamaldehyde by Huggins and Yokley's method.[1] An alternative

[1] Huggins and Yokley, *J. Amer. Chem. Soc.*, 1942, **64**, 1160.

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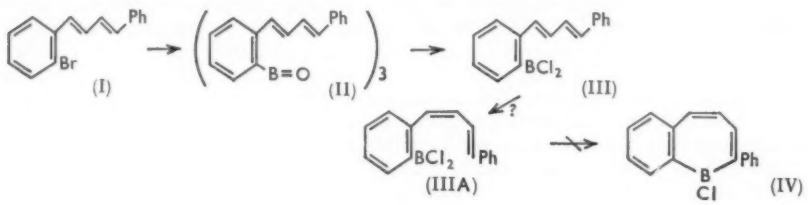
preparation, by the action of the salt from triphenylphosphine and *o*-bromobenzyl bromide on cinnamaldehyde in the presence of lithium ethoxide,[2] while more convenient, gave lower yields.

Treating of the bromo-compound (I) with a small excess of butyl-lithium, followed by butyl metaborate, gave the anhydride (II) in 12% yield. The only other product was *trans-trans*-1,4-diphenylbuta-1,3-diene (34%; identified by its m. p. and infrared spectrum), presumably obtained by hydrolysis of the unchanged lithio-compound. Attempts to improve the yield by using longer reaction times or by using the boron trifluoride–ether complex or butyl orthoborate in place of the butyl metaborate were unsuccessful. The isolation of *trans-trans*-diphenylbutadiene from this reaction suggests that both the bromo-



compound (I) and the boronic anhydride (II) have the same conformation since the reactions involved should not involve changes about the double bonds. This is supported by the absence of a band in the infrared spectra of these compounds which could be ascribed to a *cis*-ethylenic bond and by the presence of a strong band at *ca.* 10·19 μ which is characteristic of *trans*-ethylenic bonds.[3]

On treatment of boronic anhydrides with an excess of boron trichloride, exchange of oxygen with chlorine occurs;[4] it was hoped that the boronic anhydride (II) would thus afford the boron dichloride (III) and since, in the presence of catalysts such as boron halides, double bonds isomerise easily, that this would isomerise to the *cis-trans*-form (IIIA), which has the right conformation for cyclisation. Cyclisation should then occur easily by a Friedel–Crafts-type reaction[4] in the presence of catalyst, or even without it, if the resultant seven-membered ring were sufficiently stable. However, though boron trichloride in benzene caused the insoluble boronic anhydride (II) to dissolve, presumably with the formation of (III), cyclisation did not occur since only the starting material (II) was recovered from the reaction mixture. Addition of a small amount of aluminium chloride caused vigorous evolution of hydrogen chloride but gave only tars. Other attempts gave similar results.

Experimental.—1-o-*Bromophenyl*-4-*phenylbuta*-1,3-*diene* (I). A mixture of *o*-bromophenylacetic acid[6] (31·5 g.), freshly distilled cinnamaldehyde (13·0 ml.), acetic anhydride (21 ml.), and lead oxide (17 g.) was refluxed for 5 hr., then cooled and diluted with 25% acetic acid (500 ml.). A sticky solid was precipitated which was extracted with benzene. The extract was washed with dilute sodium carbonate solution, dried (Na_2CO_3), and evaporated to leave an oil, which on addition of ethanol gave pale yellow needles of 1-o-*bromophenyl*-4-*phenylbuta*-1,3-*diene* (7·2 g., 33%), m. p. 107—108° (Found: C, 67·1; H, 4·3; Br, 28·3. $C_{16}H_{13}Br$ requires C, 67·4; H, 4·6; Br, 28·1%).

o-(4-*Phenylbuta*-1,3-*dienyl*)*phenylboronic anhydride* (II). A solution of 1-*o*-bromophenyl-4-phenylbuta-1,3-diene (I) (7 g., 0·0247 mole) in benzene (50 ml.) was treated during 1 hr. at

[2] McDonald and Campbell, *J. Org. Chem.*, 1959, **24**, 1969.
[3] Bellamy, " Infra-red Spectra of Complex Molecules," J. Wiley and Sons, Inc., New York, 1954, p. 40.
[4] Gerrard and Lappert, *Chem. Rev.*, 1958, 58, 1107, and references therein.
[5] Dewar, Kubba, and Pettit, *J.*, 1958, 3073; Dewar and Dietz, *J.*, 1959, 2728; 1960, 1344.
[6] Misra and Shukla, *J. Indian Chem. Soc.*, 1951, **28**, 480.

0—10° with ethereal butyl-lithium (0·0337 mole). A solid was slowly precipitated that redissolved on addition of ethereal butyl metaborate (3·0 g. in 30 ml.) at 0°. The resultant greenish solution was refluxed for 1 hr. and left overnight, then hydrolysed with dilute hydrochloric acid. The benzene layer was dried and evaporated to leave an oil. This was chromatographed on alumina; elution with light petroleum gave *trans-trans*-1,4-diphenylbuta-1,3-diene (1·5 g., 34%), m. p. 151° (lit.,[7] 152—153°; infrared spectrum identical with that quoted [7]) (Found: C, 93·3; H, 6·8. Calc. for $C_{16}H_{14}$: C, 93·2; H, 6·8%). Elution with a large volume of chloroform for several hours gave a total of 0·7 g. (12%) of the *boronic anhydride* (II), m. p. 231° [Found: C, 82·2; H, 5·8; B, 4·6. $(C_{16}H_{13}BO)_3$ requires C, 82·8; H, 5·6; B, 4·7%], insoluble in nearly all solvents but recrystallising from a large volume of light petroleum (b. p. 100—120°). This was only very sparingly soluble in aqueous sodium hydroxide. The ultraviolet spectrum was very similar to that of *trans-trans*-1,4-diphenylbuta-1,3-diene,[8] with peaks at 332 (log ε 3·60) and 236 mμ (log ε 3·00), shoulders at *ca.* 350 (log ε 3·40) and 315 mμ (log ε 3·55), and troughs at 255 (log ε 2·30) and 220 mμ (log ε 2·85).

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Department of Chemistry, Queen Mary College, London, E.1.
[Present address: Chemistry Department, Cornell University, Ithaca, N.Y., U.S.A.] [*Received, January 6th*, 1961.]

[7] Zechmeister, *J. Amer. Chem. Soc.*, 1948, **70**, 1938; *Acta Chem. Scand.*, 1954, **8**, 1421.
[8] Friedel and Orchin, "Ulta-violet Spectra of Aromatic Compounds," J. Wiley and Sons, Inc., New York, 1951.

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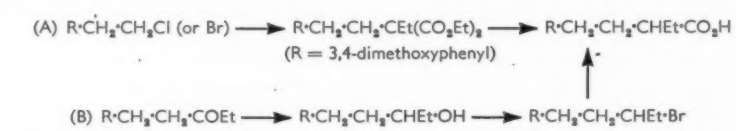
607. *Some Experiments Based on Veratraldehyde.*

By K. W. Bentley and S. F. Dyke.

In the course of other work a quantity of α-ethyl-γ-(3,4-dimethoxyphenyl)butyric acid was required, and we report two attempts to synthesise this compound, which though unsuccessful, afforded several interesting compounds.

The most obvious route to the acid involved the sequence A:


(A) R·CH₂·CH₂Cl (or Br) → R·CH₂·CH₂·CEt(CO₂Et)₂ → R·CH₂·CH₂·CHEt·CO₂H
(R = 3,4-dimethoxyphenyl)
(B) R·CH₂·CH₂·COEt → R·CH₂·CH₂·CHEt·OH → R·CH₂·CH₂·CHEt·Br

3,4-Dimethoxyphenethyl alcohol, prepared by reduction of methyl homoveratrate,[1] gave the related bromide in only 30% yield on treatment with phosphorus tribromide, but afforded the chloride in 80% yield with thionyl chloride. (These halides were further characterised by bromination to the 2-bromo-4,5-dimethoxyphenethyl halides.) Condensation of the chloride with diethyl ethylmalonate yielded only polymeric material, presumably as a result of base-catalysed elimination of hydrogen chloride followed by polymerisation of the resulting styrene.

A second route is summarised in scheme B. The bromide in this series would not react with magnesium to form the Grignard reagent, and attempts to prepare from it the related nitrile yielded only dark viscous oils.

The ketone was prepared by two routes. The condensation product of veratraldehyde and ethyl methyl ketone, which was formed in greater amount under the alkaline conditions, was hydrogenated to a saturated ketone, whose infrared spectrum was identical with that

[1] Barash and Osbond, *J.*, 1959, 2162.

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of the product obtained from β-(3,4-dimethoxyphenyl)propionyl chloride and diethylcadmium.

Experimental.—All melting points are uncorrected.

3,4-*Dimethoxyphenethyl alcohol.* Barash and Osbond's method [1] was modified slightly. The product was obtained as white crystals, m. p. 45—47° (from ether) (lit.,[1] m. p. 45—46·5°).

3,4-*Dimethylphenethyl bromide.* This was prepared essentially by Shigehiko Sugasawa's method.[2] The product was obtained as a pale yellow oil, b. p. 114—122°/0·2 mm., which slowly solidified. Crystallisation from ethanol then gave white needles, m. p. 67—68° (lit.,[2] b. p. 130—131°/0·3 mm.; m. p. 47—50°).

2-*Bromo*-3,4-*dimethoxyphenethyl bromide.* A mixture of the above ethyl bromide (16 g.) in glacial acetic acid (75 ml.) containing sodium acetate (20 g.) was cooled in ice, and bromine (10·5 g.) in glacial acetic acid (20 ml.) was added during 2 hr. The mixture was poured into water, and the precipitate extracted with chloroform. The extract was washed with aqueous sodium dithionite solution, water, 5% sodium hydrogen carbonate solution and water, then dried (Na_2SO_4). Evaporation of the solvent left a pale orange oil, which slowly solidified. Crystallisation from ethanol then yielded **2-*bromo*-3,4-*dimethoxyphenethyl bromide*** as fluffy white needles, m. p. 68—69° (Found: C, 31·8; H, 3·8; Br, 49·3. $C_{10}H_{12}Br_2O_2$ requires C, 31·7; H, 3·7; Br, 49·4%).

3,4-*Dimethoxyphenethyl chloride.* 3,4-Dimethoxyphenethyl alcohol (10 g.) in dry chloroform (50 ml.) was cooled in ice, and thionyl chloride (10 g.) in chloroform (20 ml.) was added slowly. When the vigorous evolution of hydrogen chloride ceased, the mixture was heated under reflux for 2 hr. The resulting pale brown solution was evaporated, and the residual oil was distilled under reduced pressure. The fraction (8·8 g.) of b. p. 114—116°/0·3 mm. was collected; it slowly gave clusters of elongated prisms of 3,4-dimethoxyphenethyl chloride, m. p. 52—53° (Barash and Osbond [1] give b. p. 126°/0·3 mm.) (Found: C, 60·0; H, 6·6. Calc. for $C_{10}H_{13}ClO_2$: C, 59·9; H, 6·5%).

2-*Bromo*-3,4-*dimethoxyphenethyl chloride.* This was prepared essentially as for 2-bromo-3,4-dimethoxyphenethyl bromide. The ***bromoethyl chloride*** was obtained from ethanol as white needles, m. p. 59—61° (Found: C, 43·1; H, 4·5; Br, 28·5; Cl, 12·5. $C_{10}H_{12}BrClO_2$ requires C, 43·0; H, 4·3; Br, 28·7; Cl, 12·75%).

β-(3,4-*Dimethoxyphenyl*)*propionic acid.* The corresponding cinnamic acid (obtained by a modification of the method in *Organic Syntheses* [3]) was reduced with sodium amalgam to yield the propionic acid as white needles (from water), m. p. 100—102° (lit.[4] m. p. 98°) (Found: C, 62·6; H, 6·9. Calc. for $C_{11}H_{14}O_4$: C, 62·9; H, 6·7%).

3,4-*Dimethoxyphenethyl ethyl ketone.* (*a*) From β-(3,4-dimethoxyphenyl)propionic acid. Cadmium chloride (18·5 g.) was added in one lot under nitrogen to ethylmagnesium bromide (from 4·85 g. of magnesium) in ether, and the mixture was stirred for 30 min.; Gilman's Grignard reagent test [5] was then negative. The ether was evaporated and benzene (250 ml.) was added, followed by β-(3,4-dimethoxyphenylpropionyl chloride (b. p. 139—140°/0·1 mm.; 23·0 g.) in benzene (75 ml.) during 2 min. Some heat was evolved; the mixture was stirred and heated on a water-bath for 2 hr. The complex was decomposed with 2N-sulphuric acid, the layers were separated, and the aqueous layer was extracted with benzene (2 × 150 ml.). The combined benzene solutions were washed with water, sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated to a yellow oil (21·3 g.). This was distilled and the fraction of b. p. 132—136°/0·1 mm. was collected. The infrared spectrum of this material, 3,4-dimethoxyphenethyl ethyl ketone showed a broad intense band with maximum at 1712 $cm.^{-1}$. The **2,4-*dinitrophenylhydrazone*** was obtained from ethanol as orange, fluffy needles, m. p. 139—140° (Found: C, 56·4; H, 5·5; N, 13·8. $C_{19}H_{22}N_4O_6$ requires C, 56·7; H, 5·5; N, 13·9%). The ***oxime*** crystallised from ethanol as white rods, m. p. 119—120° (Found: C, 65·9; H, 8·3; N, 5·7. $C_{13}H_{19}NO_3$ requires C, 65·9; H, 8·0; N, 5·9%).

(*b*) From veratraldehyde. (i) 2-(3,4-Dimethoxyphenyl)vinyl ethyl ketone. Veratraldehyde (140 g.) was dissolved in methanol (413 ml.), and water (650 ml.) and ethyl methyl ketone

[2] Shigehiko Sugasawa, *J. Pharm. Soc. Japan*, 1937, **57**, 296.
[3] Koo, Fish, Walker, and Blake, *Org. Synth.*, 1951, **31**, 35.
[4] Kindler and Li, *Ber.*, 1941, **74**, 321.
[5] Gilman and Schulze, *J. Amer. Chem. Soc.*, 1925, **47**, 2002.

(122 g.) were added, followed by 2N-sodium hydroxide (54 ml.). The mixture was shaken for 5 min., then kept at room temperature for 48 hr. The yellow solid was extracted with ether, and the ethereal solution dried (Na_2SO_4) and evaporated to a yellow oil (154 g.) which slowly solidified. This was distilled: the first fraction, b. p. 108—110°/0·3 mm., was unchanged veratraldehyde (30 g.), m. p. 40—43°. After a small intermediate fraction, the main fraction, b. p. 150—153°/0·3 mm., was collected (104 g.). Crystallisation from ethanol gave white rods, m. p. 83—84°, of 2-(3,4-*dimethoxyphenyl*)*vinyl ethyl ketone* (Found: C, 70·7; H, 7·4. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

(ii) 3,4-Dimethoxyphenethyl ethyl ketone. The unsaturated ketone (2·5 g.) in methanol (75 ml.) was shaken, at room temperature and atmospheric pressure, with hydrogen and palladised strontium carbonate (1·0 g.). Theoretical uptake of hydrogen (254 ml. at N.T.P. for 1 mole) occurred during 15 min., and absorption of gas ceased abruptly. The filtrate from the catalyst was evaporated to an oil. The melting-points of the 2,4-dinitrophenylhydrazone and the oxime of this material were undepressed on admixture with the corresponding derivatives of the ketone prepared from β-(3,4-dimethoxyphenyl)propionic acid.

1-(3,4-*Dimethoxyphenethyl*)*propanol*. (a) From 3,4-dimethoxyphenethyl ethyl ketone. The ketone (10 g.) in ether (70 ml.) was added to a stirred slurry of lithium aluminium hydride (2 g.) in ether (100 ml.) during 30 min. After 3 hr. the excess of lithium aluminium hydride was decomposed with dilute hydrochloric acid, and the complex with concentrated hydrochloric acid. The ether layer was separated and the aqueous layer was extracted with ether (2 × 50 ml.). The combined ethereal solutions were washed with water, dried (Na_2SO_4) and evaporated to an oil (9·5 g.) which slowly solidified. Crystallisation from light petroleum (b. p. 60—80°) gave white crystals, m. p. 36—38°, of 1-(3,4-*dimethoxyphenethyl*)*propanol* (Found: C, 69·4; H, 9·1. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%). The 3,5-*dinitrobenzoate* was obtained from ethanol as yellow prisms, m. p. 97—98° (Found: C, 57·1; H, 5·3; N, 6·7. $C_{20}H_{22}N_2O_8$ requires C, 57·4; H, 5·3; N, 6·7%).

(b) From 2-(3,4-dimethoxyphenyl)vinyl ethyl ketone. The unsaturated ketone (10 g.) in benzene (50 ml.) was added to a slurry of lithium aluminium hydride (3·5 g.) in ether (100 ml.). The mixture was warmed at 50° for 3 hr., and the product isolated as above. The infrared spectra of the two specimens were identical.

THE UNIVERSITY, OLD ABERDEEN.
THE COLLEGE OF SCIENCE AND TECHNOLOGY, BRISTOL.
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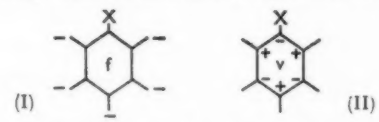
608. *Substitution Patterns of Monosubstituted Benzene Derivatives.*

By W. GERRARD, E. F. MOONEY, and H. A. WILLIS.

RANDLE and WHIFFEN [1] laid a firm foundation for the method of indicating the position of substituents in the benzene ring by using the so-called " substitution patterns " in the 800—625 cm.$^{-1}$ region. These authors assign the two prominent bands in the mono-substitution pattern to the $B_2\gamma$C–H mode or " umbrella " vibration (I) (751 ± 15 cm.$^{-1}$) and the $B_2\phi$C–H mode (II) (697 ± 11 cm.$^{-1}$). (The signs + and — indicate out-of-plane positions of the atoms.) They consider that these frequencies are substantially independent



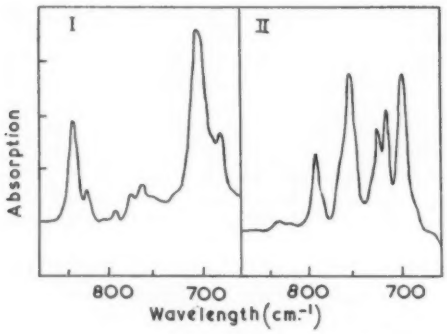
(I) (II)

of the group X. Bellamy [2] states that these bands may be influenced by electronic effects but gives little detail, while Kross, Fassel, and Margoshes [3] observe disturbance of the accepted pattern when X is a deactivating group such as NO_2 or CO_2H.

[1] Randle and Whiffen, " Molecular Spectroscopy," Institute of Petroleum, London, 1955, p. 111.
[2] Bellamy, " Infra-red Spectra of Complex Molecules," Methuen, London, 1959, p. 79.
[3] Kross, Fassel, and Margoshes, *J. Amer. Chem. Soc.*, 1956, **78**, 1332.

XUM

During our study of phenylborazole and phenylboroxole derivatives [4] it was observed that the expected substituent patterns were not obtained. No significant band near 750 cm.$^{-1}$ was found, and the striking feature in this substitution region was the very intense band centred on 705 cm.$^{-1}$. In search of the cause of the loss of the substitution pattern we re-examined many compounds with electrophilic substituents, including those previously recorded by Kross *et al.*[3] These authors illustrate the spectra of several benzoic acid derivatives, in which the high-frequency band (I; 750 cm.$^{-1}$) is very weak or absent, but in every case a low-frequency band at 710 cm.$^{-1}$ was remarkably strong; no comment was made upon this very intense band, which is the major feature of the spectra. We have examined sixteen benzoate esters, benzoic anhydride, benzoic acid and its sodium and ammonium salts, and all these show a very intense broad band in the region of 710 cm.$^{-1}$ (Table 1). When R = phenyl or phenyl-substituted alkyl or alkenyl the normal monosubstitution pattern and the " modified " pattern were superimposed.



*Infrared spectra of tri-*B*-chlorotri-*N*-phenylborazole,* (I) *as Nujol mull and* (II) *as* CS_2 *solution.*

That the modification of the substitution pattern is due to electronic interaction is clearly shown in the case of tri-*B*-chlorotri-*N*-phenylborazole, since in carbon disulphide this borazole shows the normal substitution pattern together with the doublet of the borazole ring-deformation mode. We suggest that this recovery of the normal substitution pattern is due to complex formation between carbon disulphide and the borazole derivative in which the electron-deficiency of boron is now compensated by an external co-ordination.

TABLE 1. *Substitution patterns of benzoyl derivatives,* PhCO·Y.[a]

Y	Bands (cm.$^{-1}$)	Y	Bands (cm.$^{-1}$)	Y	Bands (cm.$^{-1}$)
MeO–	One strong band 712—714	PhO–	705, 752, 692 §	$-O^-NH_4^+$	722
EtO–		$Ph·CH_2·O$–	713, 752, 698 §	Ph–	710
Pr^nO–		$Ph·CH_2·CH_2·O$–	714, 752, 701 §	Me–	763, 693
Pr^iO–		Ph·CH=CH·O–	712, 747, 692 §	H	746, 690
Bu^nO–		*o*-$Me·C_6H_4·O$–	708, 751 *		
Bu^iO–		*p*-$Me·C_6H_4·O$–	707, 805 †		
Am^iO–		–OH	712		
$C_6H_{11}O$–		Ph·CO·O	709		
Citronellyl–		$-O^-Na^+$	714		
Polyethylene glycol					

* *ortho*-Band of *o*-$Me·C_6H_4$ group. † *para*-Band of *p*-$Me·C_6H_4$ group. § Monosubstitution bands of unperturbed nucleus.

[a] There was only one strong band, at 712—714 cm.$^{-1}$, when Y was MeO, EtO, Pr^nO, Pr^iO, Bu^nO, Bu^iO, $Pr^i·[CH_2]_2·O$, $C_6H_{11}·O$, or citronellyl, and for polyethylene glycol.

The bands obtained are shown in Table 2. In tri-*B*-phenylborazole and phenylboronic anhydride, which do not form 1 : 3 complexes with nucleophiles, there is no significant difference between the spectra recorded for a Nujol mull and a carbon disulphide solution,

[4] Beck, Gerrard, Mooney, and Pratt, unpublished work.

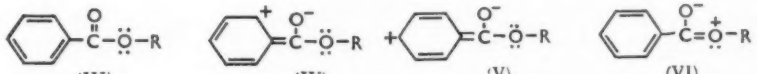
but in both cases the strong band at 708—705 cm.$^{-1}$ is present. The electronic effect is further exemplified by consideration of benzophenone, acetophenone, and benzaldehyde (Y = Ph, Me, and H respectively; Table 1). With the last two compounds, for which the normal substitution pattern is obtained, the methyl group and the hydrogen atom compensate for the $-E$ effect of the carbonyl group, so that the aromatic ring is virtually

TABLE 2. *Infrared bands (cm.$^{-1}$) of boron compounds.*

Compound	Nujol mull	CS_2 soln.
$(ClBNPh)_3$ *	759w, 704s, 690sh, 683m	754s, 724m, 715m, 701s
$(PhBNH)_3$	762w, 700s	708s (705s in tetrahydrofuran)
$(PhBO)_3$	764w, 706s	763w, 707s

* Cf. Figure.

unaffected. By a similar argument it can be seen that the alkoxy-oxygen atom plays little or no part in compensating for the $-E$ effect of the carbonyl group, that canonical forms of the type (VI) make little contribution to the structure, and that (IV) and (V) are the major canonical structures to be considered.



(III) (IV) (V) (VI)

We have observed similar effects in the substitution patterns of ring-substituted benzoate esters and acids and substituted phenylborazoles, and these results will be discussed in another paper.

Experimental.—The purity of the benzoic acid derivatives used was checked by the usual analytical methods. The borazole derivatives and phenylboronic anhydride were prepared by standard methods. The spectra were recorded as capillary films or Nujol mulls and, where stated, in solution. 0·5 mm. cells were used in a Perkin–Elmer 137 spectrometer. The calibration was checked with polystyrene, polyethylene, and ammonia.

NORTHERN POLYTECHNIC, HOLLOWAY ROAD,
LONDON, N.7.

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609. *Synthesis of 7-Fluoroflavone and Related Compounds.**

By C. T. CHANG and F. C. CHEN.

IN continuation of the synthesis of 7-halogenoflavones,[1] 7-fluoro-flavone and -flavonol and the 4′-methoxy-compounds were conveniently prepared as described previously,[1] from *m*-fluorophenyl acetate [2] by the steps shown. 7-Fluoro-4′-methoxyflavanone was also obtained by cyclization of the corresponding chalcone in phosphoric or pyrophosphoric acid, but the 7-fluoroflavanone was not available.

Experimental.—Microanalyses were by Dr. E. Aoyagi, Miike Branch, Mitsui Chemical Laboratory, Ohmuda, Japan.

4-Fluoro-2-hydroxyacetophenone (I). *m*-Fluorophenyl acetate (10 g.) and anhydrous aluminium chloride were heated at 160—170° for 2 hr., then decomposed with hydrochloric acid and steam-distilled, giving the *ketone* (8·8 g.), m. p. 24° (Found: C, 61·55; H, 4·7. $C_8H_7FO_2$ requires C, 61·9; H, 4·55%).

4′-Fluoro-2′-hydroxychalcone (II; R = H). To a cooled mixture of the above ketone (1 g.)

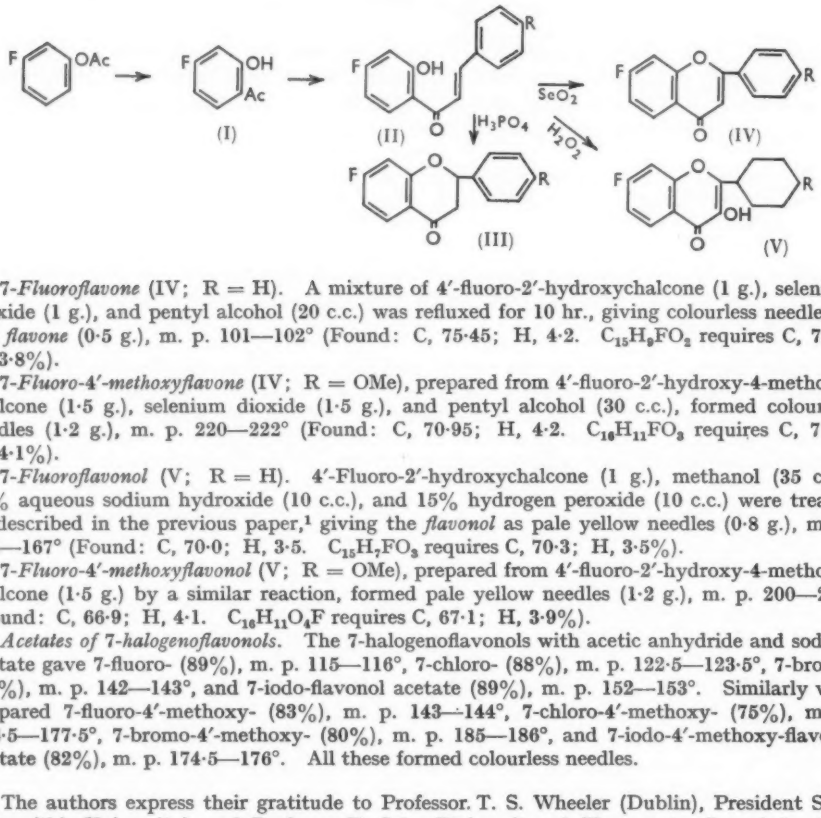
* Preliminary report see *J. Formosan Sci.*, 1958, **12**, 149.

[1] Chang and Chen, *J.*, 1958, 146.
[2] Chen, Chang, Hsu, and Lin, *J. Formosan Sci.*, 1954, **8**, 23.

and benzaldehyde (1·5 g.) in alcohol (10 c.c.) was added cold 60% aqueous potassium hydroxide (5 c.c.). The mixture was treated as stated in the previous paper,[1] giving yellow needles (1·1 g.) of the *chalcone*, m. p. 110—111° (Found: C, 74·2; H, 4·5. $C_{15}H_{11}FO_2$ requires C, 74·4; H, 4·6%).

4′-Fluoro-2′-hydroxy-4-methoxychalcone (II; R = OMe). The above ketone (I) was treated similarly with anisaldehyde, giving the *chalcone* as yellow needles (72%), m. p. 143—144° (Found: C, 70·5; H, 5·0. $C_{16}H_{13}FO_3$ requires C, 70·6; H, 4·8%).

7-Fluoro-4′-methoxyflavanone (III; R = OMe). A solution of 4′-fluoro-2′-hydroxy-4-methoxychalcone (1 g.) and phosphoric acid (*d* 1·75; 5 c.c.) in alcohol (100 c.c.) was refluxed for 72 hr. Concentration afforded a small amount of the *flavanone* as colourless needles, m. p. 90—90·5° (Found: C, 70·9; H, 5·0. $C_{16}H_{13}FO_3$ requires C, 70·6; H, 4·8%).



7-Fluoroflavone (IV; R = H). A mixture of 4′-fluoro-2′-hydroxychalcone (1 g.), selenium dioxide (1 g.), and pentyl alcohol (20 c.c.) was refluxed for 10 hr., giving colourless needles of the *flavone* (0·5 g.), m. p. 101—102° (Found: C, 75·45; H, 4·2. $C_{15}H_9FO_2$ requires C, 75·0; H, 3·8%).

7-Fluoro-4′-methoxyflavone (IV; R = OMe), prepared from 4′-fluoro-2′-hydroxy-4-methoxychalcone (1·5 g.), selenium dioxide (1·5 g.), and pentyl alcohol (30 c.c.), formed colourless needles (1·2 g.), m. p. 220—222° (Found: C, 70·95; H, 4·2. $C_{16}H_{11}FO_3$ requires C, 71·1; H, 4·1%).

7-Fluoroflavonol (V; R = H). 4′-Fluoro-2′-hydroxychalcone (1 g.), methanol (35 c.c.), 16% aqueous sodium hydroxide (10 c.c.), and 15% hydrogen peroxide (10 c.c.) were treated as described in the previous paper,[1] giving the *flavonol* as pale yellow needles (0·8 g.), m. p. 166—167° (Found: C, 70·0; H, 3·5. $C_{15}H_7FO_3$ requires C, 70·3; H, 3·5%).

7-Fluoro-4′-methoxyflavonol (V; R = OMe), prepared from 4′-fluoro-2′-hydroxy-4-methoxychalcone (1·5 g.) by a similar reaction, formed pale yellow needles (1·2 g.), m. p. 200—201° (Found: C, 66·9; H, 4·1. $C_{16}H_{11}O_4F$ requires C, 67·1; H, 3·9%).

Acetates of 7-halogenoflavonols. The 7-halogenoflavonols with acetic anhydride and sodium acetate gave 7-fluoro- (89%), m. p. 115—116°, 7-chloro- (88%), m. p. 122·5—123·5°, 7-bromo- (90%), m. p. 142—143°, and 7-iodo-flavonol acetate (89%), m. p. 152—153°. Similarly were prepared 7-fluoro-4′-methoxy- (83%), m. p. 143—144°, 7-chloro-4′-methoxy- (75%), m. p. 176·5—177·5°, 7-bromo-4′-methoxy- (80%), m. p. 185—186°, and 7-iodo-4′-methoxy-flavonol acetate (82%), m. p. 174·5—176°. All these formed colourless needles.

The authors express their gratitude to Professor. T. S. Wheeler (Dublin), President S. L. Chien (this University), and Professor E. Sebe (University of Kumamoto, Japan) for their interest and encouragement, to Mr. T. Ueng for technical assistance, and to the Asia Foundation and to the National Council on Science Development for financial support.

RESEARCH INSTITUTE OF CHEMISTRY, NATIONAL TAIWAN UNIVERSITY,
TAIPEI, FORMOSA, REPUBLIC OF CHINA. [*Received, January 13th*, 1961.]

610. *Crystallographic Examination of the α- and β-Anomers of D-Galactose.*

By B. Sheldrick.

Of the two known forms of D-galactose, the more readily obtainable α-form crystallises as a monohydrate from water and in an anhydrous form from alcohol. The latter has m. p. about 170°; its solution has an initial specific rotation of about +144° and mutarotates to +80°. The β-form [1] has an initial specific rotation of about +52° and mutarotates to +80°.

Unit-cell dimensions were published by Cox *et al.*[2] for " α-D-galactose " (obtained by the method of Riiber *et al.*[3]) and by Braekken *et al.*[4] for " stable *trans*-β-α-galactose." More recently, Werner [5] found that the interplanar spacings calculated from the published figures corresponded with the spacings obtained from a powder photograph, not of α-D-galactose, but of β-D-galactose and he suggested that Cox *et al.* had measured crystals of β-D-galactose in error. This matter has been investigated at the request of Professor E. G. Cox and Dr. T. H. Goodwin.

α- and β-Galactose have been prepared, their identities confirmed by measurement of specific rotations, and their cell dimensions measured on single crystals. The cell dimensions of α-galactose obtained were different from those given by Cox *et al.*, whereas the results for β-galactose were almost identical with those given by Cox *et al.* for α-galactose. However, large prismatic crystals found in the samples of α-galactose prepared by the method of Riiber *et al.*[3] were characterised, by microscopy and *X*-ray diffraction, not as a second crystal form of α-galactose, but as β-galactose. The fact that this can occur is now believed to have been the cause for the discrepancy.

Riiber *et al.*[3] state that E. Berner measured some crystals of β-galactose and found them to be monoclinic with axial angle $\beta = 106° 25'$ and axial ratios $a : b : c = 0{\cdot}827 : 1 : 0{\cdot}75$. These had crystallised from an aqueous solution and may, therefore, be hydrated. (There is a misprint in the reference which Braekken *et al.*[4] give to this work, the date being given as 1928 instead of 1929.)

Experimental.—*α-Galactose* (cf. Riiber *et al.*[3]). D-Galactose (10 g.) was dissolved in water (8 ml.) on a water-bath, hot absolute alcohol (120 ml.) was added, and the mixture allowed to cool slowly. The alcohol produced a heavy precipitate of microcrystalline α-galactose, which was filtered off; afterwards, on cooling, a mass of small plate-like crystals containing numerous aggregates appeared. These were not suitable for examination and a further crystallisation was carried out as follows:

D-Galactose (10 g.) was dissolved in water (12 ml.) on a water-bath, hot absolute alcohol (300 ml.) was added, and the mixture allowed to cool slowly. The crystals obtained were washed with alcohol and allowed to dry in the air. They were large and mostly intergrown, but all alike. They were similar in shape and appearance to those described by Ost [6] and a sample, dissolved in water, gave a mutarotation which confirmed that this material was α-galactose. Initially $[\alpha]_D^{21{\cdot}0}$ was +130° (Hudson and Janowsky [1] give $[\alpha]_D^{20}$ +144°).

A powder photograph of this α-galactose was obtained and the spacing calculated from it corresponded to the spacing given by Werner for α-galactose.

Single-crystal *X*-ray photographs, taken on a Weissenberg camera, showed the space group to be $P2_12_12_1$ and the cell dimensions to be: $a = 15{\cdot}78 \pm 0{\cdot}03$; $b = 7{\cdot}85 \pm 0{\cdot}02$; $c = 5{\cdot}92 \pm 0{\cdot}02$ Å. The density, measured by suspension in tetrachloroethane–tetrachloroethylene, was $1{\cdot}60_1$ g./ml. This gave a cell weight of 706 and a molecular weight of 177 (Calc. for $C_6H_{12}O_6$: *M*, 180). The α-galactose examined was therefore anhydrous.

[1] Hudson and Janowsky, *J. Amer. Chem. Soc.*, 1917, **39**, 1021.
[2] Cox, Goodwin, and Wagstaff, *J.*, 1935, 978.
[3] Riiber, Minsaas, and Lyche, *J.*, 1929, 2173.
[4] Braekken, Koren, and Sørensen, *Z. Krist.*, 1934, **88**, 205.
[5] Werner, *Mikrochem.*, 1952, **39**, 133.
[6] Ost, *Z. analyt. Chem.*, 1890, **29**, 651.

XUM

The crystal faces present were {011} in addition to {100}, {010} and {001}.

β-*Galactose* (cf. Hudson and Janowsky [1]). D-Galactose (8 g.) was dissolved in hot water, cooled to 0°, and poured, with stirring, into absolute alcohol (200 ml.) previously cooled in ice–salt. The crystals produced were washed quickly with cold alcohol and allowed to dry. They were prismatic, quite different from the flat plates of the α-form, and had faces of the type {201} and {210}. A sample mutarotated in water in the direction required for β-galactose, and a powder photograph gave spacings in agreement with those given by Werner for β-galactose.

Single-crystal *X*-ray photographs, taken on a Weissenberg camera, showed the space group to be $P2_12_12_1$ and the cell dimensions to be: $a = 12{\cdot}67 \pm 0{\cdot}03$; $b = 7{\cdot}77 \pm 0{\cdot}02$; $c = 7{\cdot}68 \pm 0{\cdot}02$ Å. The cell dimensions given by Cox *et al.*,[2] supposedly for α-galactose, were: $a = 12{\cdot}68$; $b = 7{\cdot}78$; $c = 7{\cdot}71$ Å.

The density was $1{\cdot}61_3$ g./ml., which gave a cell weight of 727 and $M = 182$; hence this β-galactose was anhydrous.

Microscopic examination of the first batch of α-galactose prepared by the method of Riiber *et al.* showed that it contained some large prismatic crystals, usually at the centre of aggregates of the smaller, plate-like crystals. Riiber *et al.* themselves noted this fact. Some of these prismatic crystals were separated and measured. Single-crystal *X*-ray rotation photographs showed them to have the cell dimensions of β-galactose. Measurement of the interfacial angles confirmed the presence of faces of the types {201}, {110}, and {210}.

The author thanks Professor E. G. Cox for his suggestions and provision of facilities for this work, and Dr. J. H. Robertson for his advice.

Department of Inorganic and Structural Chemistry,
The University, Leeds, 2. [*Received, December 22nd,* 1960.]

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611. *Hydrolysis of* N-*Acylphosphoramidic Acids. Part IV.*[1] N-*Benzenesulphonylphosphoramidic Acid.*

By M. Halmann, A. Lapidot, and David Samuel.

N-Substituted phosphoramidic acids are hydrolysed in aqueous solution to phosphoric acid and an amide or amine. Previous papers in this series have shown that the rates of hydrolysis are maximal at about pH 4.[1,2] At this pH the compounds are mostly in the monoanion form, indicating that an acidic proton is required for solvolysis, as has been suggested for monoalkyl phosphates.[3] In the more acid range, below pH 1, *N*-substituted phosphoramidic acids show differences in rate and in the effect of acids, depending on the substituting group. Hydrolyses of phenyl, *p*-methoxyphenyl, and unsubstituted phosphoramidic acids $R{\cdot}NH{\cdot}PO(OH)_2$ are strongly catalysed by acids,[4] whereas the *N*-acylphosphoramidic acids investigated, *i.e.*, those with a carbonyl or phosphoryl group adjacent to the nitrogen atom, are not susceptible to acid catalysis. It was suggested [1] that this may be due to the marked polarity of the carbonyl and phosphoryl groups which causes withdrawal of negative charge from the nitrogen of the phosphoramidic acid and makes it less susceptible to protonation. This interpretation was supported by the observation that the *N*-acylphosphoramidic acids, phosphourethane $C_2H_5{\cdot}CO{\cdot}NH{\cdot}PO(OH)_2$, and diphenyl *N*-dihydroxyphosphinylphosphoramidate $(PhO)_2PO{\cdot}NH{\cdot}PO(OH)_2$ are hydrolysed at the same rates in water and in deuterium oxide, presumably since there is no protonation of nitrogen in acid solution (to form the conjugate acid). We have now tested this hypothesis by examining the hydrolysis of another phosphoramidic acid with a highly polar acyl group, benzenesulphonyl, in the presence of acid and also in D_2O.

[1] Part III, Halmann, Lapidot, and Samuel, *J.*, 1960, 4672.
[2] (*a*) Lapidot and Halmann, *J.*, 1958, 1713; (*b*) Halmann and Lapidot, *J.*, 1960, 419.
[3] Westheimer, *Chem. Soc. Spec. Publ.*, No. 8, 1957, p. 1; Vernon, *ibid.*, p. 17.
[4] Chanley and Feageson, *J. Amer. Chem. Soc.*, 1958, **80**, 2686; Winnick and Scott, *Arch. Biochem. Biophys.*, 1947, **12**, 201; Rathler and Rosenberg, *ibid.*, 1956, **65**, 319.

N-Benzenesulphonylphosphoramidic acid,[5] $Ph{\cdot}SO_2{\cdot}NH{\cdot}PO(OH)_2$, was found to hydrolyse smoothly to benzenesulphonamide and phosphoric acid. The rates of hydrolysis determined at various pH's and temperatures are summarised in Table 1. From the temperature-dependence of the rate of hydrolysis, the energy and entropy of activation at pH 4 were calculated: $\Delta E^* = 26{\cdot}1$ kcal./mole; $\Delta S^* = +0{\cdot}56$ e.u. These values are very

TABLE 1. *Hydrolysis of* N-*benzenesulphonylphosphoramidic acid* [10^4k (*obs.*) (*sec.*$^{-1}$)].

Solvent	$HClO_4$ 8·3M	$HClO_4$ 5·8M	KHP * 0·05M	DB * 0·05M	$Na_2B_4O_7$ 0·5M
pH			4·02	7·4	9·07
60·0°	1·13	1·32	8·9	0·94	0·013
50·0°			3·31		
37·0°			0·55		

* KPH = KH phthalate. DB = diethyl barbiturate.

similar to those found for other phosphoramidic acids.[1,2] The rates of hydrolysis in water and in deuterium oxide were determined at pH 4 and in 0·1M-sulphuric acid (or deuterosulphuric acid) at 50° and at 60°. The results are given in Table 2.

Table 1 shows that at 60° there is a maximum in the rate at pH 4, as with other substituted phosphoramidic acids. The dissociation constants of *N*-benzenesulphonylphosphoramidic acid at 25° were $K_1 = (1{\cdot}49 \pm 0{\cdot}09) \times 10^{-4}$, $K_2 = (7{\cdot}72 \pm 0{\cdot}12) \times 10^{-8}$, indicating again that the monoanion is the active species in hydrolysis. On the other hand, as shown in Table 1, there is *no* catalysis by acids even in 8M-perchloric acid. This is due to prevention of protonation on the amido-nitrogen by the very polar sulphonyl group. It is further confirmed by the total absence of a deuterium isotope effect on hydrolysis shown in Table 2.

From these results and those of previous papers in this series,[1,2,4] the susceptibility to acid catalysis is seen to decrease in the order, $Ar{\cdot}NH{\cdot}PO(OH)_2$, $Ph{\cdot}CO{\cdot}NH{\cdot}PO(OH)_2$, $EtO_2C{\cdot}NH{\cdot}PO(OH)_2$, $(PhO)_2PO{\cdot}NH{\cdot}PO(OH)_2$, $Ph{\cdot}SO_2{\cdot}NH{\cdot}PO(OH)_2$. *N*-Benzoylphos-

TABLE 2. *Solvolysis of* N-*benzenesulphonylphosphoramidate in water and* D_2O [10^4k (*obs.*) (*sec.*$^{-1}$)].

Solvent	Temp.	H_2O	D_2O
K H Phthalate (0·05M)	50·0°	3·31 ± 0·01	3·36 ± 0·02
Sulphuric acid (0·1M)	60·0°	5·65 ± 0·03	5·65 ± 0·01

phoramidic acid will undergo acid catalysis in very concentrated acid, possibly because the phenyl group reduces the electron-deficiency at the carbonyl-carbon atom. In the *N*-benzenesulphonyl compound, however, it appears that the polarity of the sulphonyl group is such that the phenyl group has no effect and acid catalysis is prevented even at very high acidities (8M).

Experimental.—*N*-Benzenesulphonylphosphoramidic acid was prepared according to directions of Kirsanov and Abrazhanova [5] and after two washings with anhydrous ether had m. p. 149—150° (Found: P, 13·15. Calc. for $C_6H_8NO_5PS$: P, 13·1%). The dissociation constants at 25° were determined by the Henderson equation, $pK = -\log [H^+][B + H^+]/(C - [B + H^+])$, from the titration curve with sodium hydroxide; a Radiometer glass electrode pH-meter was used.

The products of hydrolysis were benzenesulphonamide, m. p. 156°, and phosphoric acid (yield, determined colorimetrically, 100 ± 1%).

Kinetic experiments. The *N*-benzenesulphonylphosphoramidic acid (20—30 mg.) in aqueous buffer or acid solution (25 ml.) was kept in a thermostat and at intervals, aliquot parts were withdrawn for determination of phosphate by Fiske and Subbarow's method.[6] Runs were

[5] Kirsanov and Abrazhanova, *Sbornik Statei Obshchei Khim.*, 1953, **2**, 1048.
[6] Fiske and Subbarow, *J. Biol. Chem.*, 1925, **66**, 375.

XUM

made at least in duplicate and rate constants were calculated for first-order reactions. D_2O containing sulphuric acid (0·1M) was prepared from deuterosulphuric acid (Fluka) and deuterium oxide (Norsk-Hydro).

This investigation was supported in part by a grant RG-5842 from the Division of Research Grants, U.S. Public Health Service.

THE ISOTOPE DEPT., THE WEIZMANN INSTITUTE OF SCIENCE,
REHOVOTH, ISRAEL. [*Received, January 27th*, 1961.]

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612. *A Simple Synthesis of αβ-Dialkylacrylic Acids.*

By ISRAEL SHAHAK.

IT has been found [1] that β-alkyl-α-fluoroacrylic acids can be prepared easily and in good yield by condensation of aldehydes with diethyl α-fluoro-oxaloacetate without isolation of any of the intermediate compounds or even the keto-ester itself:

$$R{\cdot}CHO + EtO_2C{\cdot}CO{\cdot}CHF{\cdot}CO_2Et \longrightarrow R{\cdot}CH{:}CF{\cdot}CO_2H$$

It seemed worthwhile to apply the same principle to the synthesis of αβ-dialkylated acrylic acids from diethyl α-alkyloxaloacetates. This has been achieved, with overall yields of 70—75% based on the initial ester. The systems studied were ethyl propionate with benzaldehyde and heptaldehyde, and ethyl butyrate with heptaldehyde. For comparison the condensation of ethyl α-ethoxalyl-propionate, -butyrate, and -phenylacetate with benzaldehyde was investigated; *i.e.*, in these cases the intermediate derivative was isolated. The yields in the condensation with benzaldehyde were of the order of 90%.

The keto-esters used here were less reactive than diethyl α-fluoro-oxaloacetate: whilst the latter reacted in ether or tetrahydrofuran, boiling xylene or dibutyl ether (about 140°) had to be used in the present cases.

The products were identified by comparison with authentic specimens; in one instance, the substituted acrylic acid was hydrogenated to the known corresponding saturated acid. The ultraviolet spectra of ethyl 2-methyl- ($\lambda_{max.}$ 221 mμ; log ε 4·08) and 2-ethyl-non-2-enoate ($\lambda_{max.}$ 220 mμ; log ε 4·00) (both in ethanol) also showed that the acids obtained were αβ-unsaturated; their spectrum is that of crotonic acid,[2] but shifted bathochromically by the β-alkyl groups. In the infrared spectra of the two compounds, the carbonyl absorption was at 1707 cm.$^{-1}$, that of the C=C double bond at 1661 cm.$^{-1}$.

The condensation of α-alkyloxaloacetates with formaldehyde [3] and aromatic aldehydes [4] has been studied before, but only up to the first step of β-ethoxycarbonyl-α-oxo-γ-butyrolactones (hydrogen or aryl in β-position).

Experimental.—Ethyl α-methylcinnamate. (*a*) Diethyl oxalate (15 g.) and ethyl propionate (10·2 g.) were added successively to a suspension of sodium hydride (2·4 g.) or sodium ethoxide (6·8 g.) in dibutyl ether or xylene (150 ml.); after 1 hr, at 50°, the mixture was heated at 70°/35 mm. until the ethanol had distilled off and the b. p. of dibutyl ether (or xylene) had been reached. Usually, the enolate of ethyl α-ethoxalylpropionate separated. After 30 min. at 50°, freshly distilled benzaldehyde (10·6 g.) was added and the mixture refluxed for 1 hr. The enolate disappeared, and the product gradually crystallized. The mixture was poured into water, and the organic layer washed with 7% sodium carbonate solution and water, dried, and concentrated at 35 mm. The residual ester (12 g., 63%) distilled at 124—125°/1 mm. Its hydrolysis gave α-methylcinnamic acid, m. p. and mixed m. p. 81°.[5] This acid was further hydrogenated in

[1] Bergmann and Shahak, *J.*, in the press.
[2] Hausser, Kuhn, Smakula, and Hoffer, *Z. phys. Chem.*, 1935, *B*, **29**, 371.
[3] Schinz and Hinder, *Helv. Chim. Acta*, 1947, **30**, 1349.
[4] Labib, *Compt. rend.*, 1957, **244**, 2396.
[5] Raikov, *Ber.*, 1887, **20**, 3396.

the presence of platinum oxide as catalyst to α-methyl-β-phenylpropionic acid, b. p. 142°/2 mm., m. p. 36° [6] (amide, m. p. 110°).

(*b*) From ethyl α-ethoxalylpropionate [7] (20·2 g.) and sodium hydride (2·4 g.), the enolate was prepared in xylene (150 ml.). When all the sodium hydride had reacted, benzaldehyde (10·6 g.) was added and the preparation continued as above. The yield of the ester was 18·5 g. (97%).

Ethyl α-ethylcinnamate. (*a*) This ester was prepared analogously, from ethyl butyrate, diethyl oxalate, and benzaldehyde, the yield being 15 g. (74%), and the b. p. 122—123°/1 mm. Hydrolysis gave the known *trans*-α-ethylcinnamic acid,[8] m. p. 104°.

(*b*) When ethyl α-ethoxalylbutyrate [9] (21·6 g.) was employed in xylene (150 ml.), ethyl α-ethylcinnamate was obtained in 94% yield (19 g.).

Ethyl 2-methylnon-2-enoate, obtained in 93% yield from ethyl propionate and heptaldehyde, had b. p. 93—95°/2 mm. (Found: C, 72·9; H, 11·3. $C_{12}H_{22}O_2$ requires C, 72·7; H, 11·1%).

Ethyl 2-ethylnon-2-enoate, prepared in 95% yield from ethyl butyrate and heptaldehyde, had b. p. 95—98°/2 mm. (Found: C, 73·2; H, 11·6. $C_{13}H_{24}O_2$ requires C, 73·6; H, 11·3%).

Ethyl α-phenylcinnamate. (*a*) As described above, ethyl phenylacetate (18·4 g.) and diethyl oxalate (15 g.) were condensed by means of sodium hydride (2·4 g.) in dibutyl ether (500 ml.), and benzaldehyde (10·6 g.) was added. The ester (20·5 g., 81%) boiled at 163—165°/1 mm. Hydrolysis gave *trans*-α-phenylcinnamic acid,[10] m. p. 172°.

(*b*) Ethyl sodio-α-ethoxyalyl-α-phenylacetate [11] (28·6 g.) was suspended in xylene (150 ml.), benzaldehyde (10·6 g.) added, and the mixture refluxed for 1 hr. The yield of ethyl α-phenylcinnamate was 91% (23 g.).

DEPARTMENT OF ORGANIC CHEMISTRY,
HEBREW UNIVERSITY, JERUSALEM.

[*Received, January 30th*, 1961.]

[6] Conrad and Bischoff, *Annalen*, 1880, **204**, 194.
[7] *Org. Synth.*, Coll. Vol. II, p. 272.
[8] Claisen, *Ber.*, 1890, **23**, 976.
[9] Adickes and Andresen, *Annalen*, 1943, **555**, 41.
[10] Mueller, *Ber.*, 1893, **26**, 659.
[11] Wislicenus, *Ber.*, 1894, **27**, 1092.

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613. *Degradative Studies of Peptides and Proteins. Part VI.*[1] *The Cyclisation and Degradation of N-Phenylthiocarbamoylsarcosine Derivatives.*

By D. T. ELMORE.

IT has been shown that anhydrous acids degrade *N*-phenyl- and *N*-acyl-thiocarbamoyl-peptides (I; R^1 = Ph or acyl) to salts of 2-anilino- and 2-acylamino-thiazol-5-ones (II; R^1 = Ph or acyl) respectively.[2,3] Since, however, *N*-acylthiocarbamoyl derivatives of sarcosine (III; R^1 = acyl) afford 2-acylimino-3-methylthiazolid-5-ones (IV; R^1 = acyl),[1] we decided to study the degradation of *N*-phenylthiocarbamoylsarcosine derivatives (III; R^1 = Ph). The amide and benzylamide of *N*-phenylthiocarbamoylsarcosine (III; R^1 = Ph, R^2 = NH_2 or $NH{\cdot}CH_2Ph$) were synthesised from phenyl isothiocyanate and the corresponding sarcosine derivatives. Cyclisation occurred with astonishing ease, either on brief warming or on treatment with cold trifluoroacetic acid. The product in both cases was 1-methyl-3-phenyl-2-thiohydantoin (V; R^1 = Ph), identical with a synthetic sample;[4] there was no sign of an intermediate 2-anilino-3-methylthiazolid-5-one. Rearrangement of *N*-substituted 2-iminothiazolid-5-ones to 2-thiohydantoins is probably facilitated by a high electron-density on the imino-nitrogen atom. Since this is diminished by resonance with the adjacent carbonyl group in 2-acyliminothiazolid-5-ones, the relative stability of

[1] Part V, Elmore, *J.*, 1959, 3152.
[2] Edman, *Nature*, 1956, **177**, 667; *Acta Chem. Scand.*, 1956, **10**, 761.
[3] Elmore and Toseland, *J.*, 1957, 2460.
[4] Cook and Cox, *J.*, 1949, 2342.

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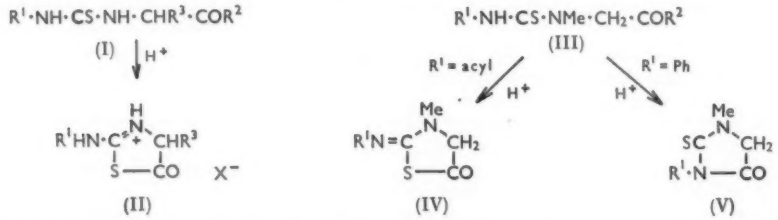
the latter and the absence of a corresponding intermediate in the degradation of *N*-phenylthiocarbamoylsarcosine derivatives can be explained.

It is of interest to note that a strong " thioureide " band at 1518 cm.$^{-1}$ is present in the



infrared spectrum of 1-methyl-3-phenyl-2-thiohydantoin. This is additional evidence in support of the suggestion [5] that this feature of the spectra of compounds containing the >N·C:S system is not due solely to a δNH frequency.

Experimental.—*N-Phenylthiocarbamoylsarcosine amide.* Sarcosine amide (from 3·72 g. of the hydrogen sulphate [6]) in a mixture of dry ether (5 c.c.) and chloroform (5 c.c.) was treated with phenyl isothiocyanate (2·70 g.) in ether (5 c.c.). The crystalline *N-phenylthiocarbamoyl derivative* (3·97 g.), which separated, had m. p. 156—158° (decomp.) (Found: C, 53·6; H, 5·55; N, 19·05. $C_{10}H_{13}N_3OS$ requires C, 53·8; H, 5·9; N, 18·8%). In warm ethanol, acetonitrile, or cold pyridine, ammonia was evolved. From ethanol, 1-methyl-3-phenyl-2-thiohydantoin was obtained, m. p. and mixed m. p. 160·5—161·0°. 1-Methyl-3-phenyl-2-thiohydantoin in methanol had $\lambda_{max.}$ 266·5 (ε 14,100) and 235 (ε 10,700), $\lambda_{min.}$ 248 (ε 8600) and 222—226 mμ (ε 10,200).[7]

N-Phenylthiocarbamoylsarcosine benzylamide. Sarcosine benzylamide (from 2·60 g. of the hydrobromide [1]) in ether (20 c.c.) was treated with phenyl isothiocyanate (1·35 g.) in ether (20 c.c.). The *product* (3·06 g.), after crystallisation from ethanol with the minimum of heating, had m. p. 128—129° (Found: C, 65·3; H, 6·4; N, 13·7. $C_{17}H_{19}N_3OS$ requires C, 65·1; H, 6·1; N, 13·4%). On one occasion, attempted recrystallisation of the crude product afforded 1-methyl-3-phenyl-2-thiohydantoin, m. p. and mixed m. p. 160—161°. The benzylamide (0·626 g.) was left in trifluoroacetic acid (2 c.c.) for 40 hr. After evaporation, addition of water afforded the thiohydantoin (0·350 g.), which had m. p. and mixed m. p. 160·5—161·0° after recrystallisation.

DEPARTMENT OF BIOCHEMISTRY, QUEEN'S UNIVERSITY, BELFAST.

[*Received, February 2nd,* 1961.]

[5] Elmore, *J.*, 1958, 3489.
[6] Cook and Cox, *J.*, 1949, 2334.
[7] Edward and Nielsen, *J.*, 1957, 1014.

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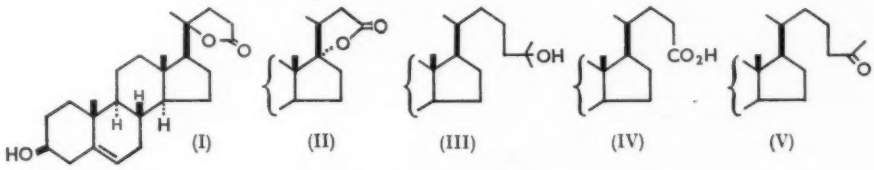
614. *Hydroxylation of 5α,6β-Dibromocholestan-3β-yl Acetate by Chromic Acid.*

By A. L. J. BECKWITH.

OXIDATION of 5α,6β-dibromocholestane-3β-yl acetate, the key reaction in the preparation of steroid hormones from cholesterol, has been the subject of numerous investigations.[1] The major products obtained after debromination and hydrolysis are 3β-hydroxyandrost-5-en-17-one (2—8%) and 3β-hydroxypregn-5-en-20-one, but a number of other products, most of which are formed by oxidative degradation of the side chain, have also been isolated. It has been suggested [1,2] that the initial step is a hydroxylation, occurring most

[1] See Fieser and Fieser, " Steroids," Reinhold Publ. Corp., New York, 1959, pp. 508—511.
[2] Billeter and Miescher, *Helv. Chim. Acta*, 1947, **30**, 1409.

readily at tertiary positions, a hypothesis supported by the formation of the lactone (I) of 3β,20ξ-dihydroxychol-5-enoic acid.[2,3] Similarly, oxidation of sitosterol acetate dibromide yields the lactone (II) of 3β,17α-dihydroxy-23-norchol-5-enoic acid.[4]



(I) (II) (III) (IV) (V)

Additional evidence for a mechanism involving hydroxylation has now been obtained. After debromination and hydrolysis of the crude product from oxidation of 5α,6β-dibromocholestan-3β-yl acetate with chromium trioxide in acetic acid [5] the neutral fraction was distributed between hexane and 92% aqueous methanol. The material from the polar phase, when chromatographed on alumina, yielded cholest-5-ene-3β,25-diol (III) which was identified by preparation of the mono- and the di-acetate.[6] A very small amount of an unidentified triol, $C_{27}H_{46}O_3$, was also isolated.

The formation of the diol (III) in relatively high yield (2%, calculated on unrecovered cholesterol) indicates that it is possibly a precursor of the previously isolated products, 3β-hydroxychol-5-enoic acid [5,7] (IV) and 3β-hydroxy-27-norcholest-5-en-25-one [8] (V), both of which may be formed by dehydration of the tertiary alcohol followed by oxidation of the double bond. The ready hydroxylation at the 25-position is in accord with the formation of cholest-5-ene-3β,25-diol by aerial oxidation of cholesterol.[9]

Experimental.—3β-Acetoxy-5α,6β-dibromocholestane (28 g.) was oxidised with chromium trioxide (48 g.) in acetic acid.[5] After debromination with zinc dust (30 g.) in acetic acid (200 ml.) the crude product, dissolved in ether, was extracted with 2N-aqueous sodium hydroxide. Acidification of the aqueous extract yielded a mixture of acids (2·8 g.). Evaporation of the ethereal solution afforded a gum (13·7 g.) which was heated under reflux with potassium hydroxide (10 g.) in methanol (250 ml.) for 2 hr. Cholesterol (7·4 g.), which crystallised from the cooled reaction mixture, was collected and the filtrate and washings were evaporated. The residue (4·9 g.) was distributed between hexane and 92% methanol (3 × 60 ml. of each solvent) in separatory funnels, and the methanol-soluble material (1·76 g.) was chromatographed on alumina. Gradient elution with ether–hexane gave the following fractions:

(i) Cholest-5-ene-3β,25-diol (180 mg.) which crystallised from ether–hexane in prisms, m. p. 178—180°, $[\alpha]_D^{20}$ −38° (lit.,[5] m. p. 177—179°, 181·5—182·5°, $[\alpha]_D^{19}$ −39·3°, $[\alpha]_D^{25}$ −38·6°) (Found: C, 80·4; H, 11·5. Calc. for $C_{27}H_{46}O_2$: C, 80·5; H, 11·5%). The monoacetate prepared by treatment of the diol with pyridine and acetic anhydride at 0° formed needles (from methanol), m. p. 140—142°, $[\alpha]_D^{20}$ −42° (lit.,[5] m. p. 138—140°, 140—141°, $[\alpha]_D^{19}$ −40·4°, $[\alpha]_D^{25}$ −42·1°) (Found: C, 78·0; H, 10·8. Calc. for $C_{29}H_{48}O_2$: C, 78·3; H, 10·9%). Acetylation of the monoacetate with the same reagents under reflux yielded the diacetate which crystallised from methanol in plates, m. p. 119—120°, $[\alpha]_D^{25}$ −35° (lit.,[5] m. p. 119·5—120°, $[\alpha]_D^{25}$ −35·5°) (Found: C, 76·5; H, 10·6. Calc. for $C_{31}H_{50}O_4$: C, 76·5; H, 10·4%). Treatment of the diol with pyridine and benzoyl chloride at 100° for 1 hr. afforded the *dibenzoate*, laths (from ethanol), m. p. 100—102°, $[\alpha]_D^{20}$ −10° (Found: C, 80·7; H, 9·0. $C_{41}H_{54}O_4$ requires

[2] Miescher and Fischer, *Helv. Chim. Acta*, 1939, **22**, 155; Billeter and Miescher, *ibid.*, 1949, **32**, 564; Ryer and Gebert, *J. Amer. Chem. Soc.*, 1952, **74**, 4336.
[4] Ryer and Gebert, *J. Amer. Chem. Soc.*, 1952, **74**, 41.
[5] Wallis and Fernholz, *J. Amer. Chem. Soc.*, 1935, **57**, 1504.
[6] Ryer, Gebert, and Murrill, *J. Amer. Chem. Soc.*, 1950, **72**, 4247; Dauben and Bradlow, *ibid.*, p. 4248.
[7] Ruzicka and Wettstein, *Helv. Chim. Acta*, 1935, **18**, 986.
[8] Ruzicka and Fischer, *Helv. Chim. Acta*, 1937, **20**, 1291.
[9] Fieser, Huang, and Bhattacharyya, *J. Org. Chem.*, 1957, **22**, 1380; Beckwith, *Proc. Chem. Soc.* 1958, 194.

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C, 80·6; H, 8·9%). A similar benzoylation at 0° yielded a *monobenzoate*, as rods (from hexane), m. p. 176—178°, $[\alpha]_D^{25}$ −13° (Found: C, 80·4; H, 9·8. $C_{34}H_{50}O_3$ requires C, 80·6; H, 9·9%).

(ii) An unidentified *triol* (65 mg.) which crystallised from aqueous methanol in plates, m. p. 192° (Found: C, 77·1; H, 11·0. $C_{27}H_{46}O_3$ requires C, 77·45; H, 11·1%). The *diacetate* crystallised from aqueous methanol in rods, m. p. 137° (Found: C, 74·0; H, 10·1. $C_{31}H_{50}O_5$ requires C, 74·1; H, 10·0%).

(iii) Cholestane-3β,5α,6β-triol (18 mg.), identical with an authentic specimen.

UNIVERSITY OF ADELAIDE, ADELAIDE,
SOUTH AUSTRALIA.

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615. *The Reaction of Dialkyl Phosphites and Trialkyl Phosphates with Sodium* NN-*Diethyldithiocarbamate.*

By T. D. SMITH.

As part of a study of salts of organic phosphorus acids the reaction of dialkyl phosphites with salts of *NN*-diethyldithiocarbamic acid was investigated. This may be represented as: $PHO(OR)_2 + NEt_2{\cdot}CS{\cdot}SNa \longrightarrow PHO(OR){\cdot}ONa + NEt_2{\cdot}CS_2R$. With dimethyl phosphite the reaction was complete within minutes, but for higher alkyl phosphites required some hours. Zinc diethyldithiocarbamate yielded zinc monoalkyl phosphites and the corresponding ester of diethyldithiocarbamate, though reaction, even in the case of dimethyl phosphite, required a higher temperature.

It has been noted in the alkylation of thiourea [1] that trialkyl phosphates are as effective alkylating agents as dialkyl phosphites. Reaction of trialkyl phosphates with sodium diethyldithiocarbamate gave the sodium dialkyl phosphate and the diethyldithiocarbamate ester. Again reaction with trimethyl phosphate was complete within minutes, but higher alkyl phosphates required prolonged heating at 100°.

General methods for the preparation of esters of dialkylthiocarbamic acids include treatment of the aqueous sodium salt with alkyl halides [2] and reaction of the free acid with a compound having an activated C–C double bond to which the dithiocarbamic acid adds.[3] The present work establishes a further method for the preparation of the n-alkyl esters. Sodium monoalkyl phosphites have been obtained by treatment of the dialkyl phosphites with 1 mol. of sodium hydroxide in aqueous alcohol followed by evaporation in a vacuum.[4] Alternatively treatment of sodium dialkyl phosphites with 1 mol. of water in dry alcohol results in good yields of the sodium monoalkyl phosphites. Reaction of dialkyl phosphites with sodium diethyldithiocarbamate results in a convenient preparation of the sodium salt of the monoalkyl phosphite in good yield.

Experimental.—Sodium *NN*-diethyldithiocarbamate (0·5 mole) was heated at 100° with the dialkyl phosphite (0·5 mole) for 4 hr. during which there was no loss in weight though during the early stages an ammoniacal odour developed. The mixture separated into two phases, completion of reaction being noted by treating samples of both phases with an aqueous solution of cupric chloride which detects extremely small quantities of diethyldithiocarbamate. When an excess of dialkyl phosphite was used the remaining dialkyl phosphite appeared almost completely in the upper phase. The lower phase was separated and treated with 200 ml. of acetone; the sodium monoalkyl phosphite separated. After filtration the residue was washed with dry ether and the salt recrystallised from ethanol.

The filtrate was evaporated to remove acetone, and the residue combined with the upper phase and washed with 10% aqueous potassium carbonate (2 × 200 ml.). The ester was finally

[1] Smith and Parker, *J.*, 1961, 442.
[2] Campbell and Tyson, *Ind. Eng. Chem.*, 1953, **45**, 125.
[3] Hook, Beegle, and Wystrach, U.S.P. 2,786,866.
[4] Nylen, *Svensk Kem. Tidskr.*, 1936, **48**, 2.

washed with hot water and distilled at low pressure.[2] The salient features of the various syntheses are detailed in the annexed Table. From dimethyl phosphite the sodium salt was

Product	Yield (%)	M. p.	Found (%) C	H	P or S	N	Required (%) C	H	P or S	N
$NaBuHPO_4$	69	177°	33·0	6·9	22·1		33·1	6·9	22·1	
$NaEtHPO_4$	71	183	20·3	5·0	26·4		20·6	5·2	26·7	
$NEt_3 \cdot CS_2Bu$	64		53·1	9·4	30·9	6·8	52·7	9·3	31·2	6·8
$NEt_3 \cdot CS_2Et$	79		47·5	8·5	36·0	7·85	47·45	8·5	33·2	7·9
$NEt_3 \cdot CS_2Me$	94		43·9	8·0	39·1	8·55	44·2	8·0	39·3	8·6

obtained as a very hygroscopic solid. Of the trialkyl phosphates used trimethyl phosphate reacted most readily, though in all cases the reaction was carried out under reflux with a small flame.

Department of Chemistry,
University College of North Wales,
Bangor, Caern.

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616. *Interaction between Selenium Oxychloride and the Trichlorides of Boron and Aluminium.*

By M. J. Frazer.

Many metal and non-metal chlorides dissolve in selenium oxychloride,[1] and these solutions have been of interest in connection with theories of acid and base behaviour in aprotic solvents.[2] Only a few solid solvates ($SnCl_4,2X$;[3,4] $SbCl_5,X$;[4] $ZrCl_4,2X$;[5] where $X = SeOCl_2$) have been isolated; but the solids isolated from selenium oxychloride solutions of phosphorus trichloride and pentachloride,[6] silicon tetrachloride,[3] and titanium tetrachloride [3] contain selenium tetrachloride.

Selenium oxychloride, when mixed with boron trichloride or aluminium trichloride in methylene chloride, gave a precipitate, which analysis indicated to be either the addition compound $2MCl_3,3SeOCl_2$ or the products of the reaction: $2MCl_3 + 3SeOCl_2 \longrightarrow M_2O_3 + 3SeCl_4$, where M = B or Al. The precipitate was formed immediately with boron trichloride but more slowly in the second experiment, probably owing to the insolubility of aluminium chloride in methylene chloride. Vacuum-sublimation of the precipitates gave selenium tetrachloride and a residue of boric or aluminium oxide. Additional evidence that there was reaction and not formation of an addition compound came from the infrared spectra of the original precipitates, which did not show bands in the region from 800—975 cm.$^{-1}$ which have been attributed to the Se=O bond in selenium oxychloride and its complexes.[3] Absorption bands between 1400 and 1180 cm.$^{-1}$ in the boron trichloride experiment, and continuous absorption between 900 and 650 cm.$^{-1}$ in the aluminium trichloride experiment, indicated the formation of metal–oxygen links.

Experimental.—Selenium oxychloride (10·38 g., 2 mol.) and boron trichloride (1 mol.) were mixed in methylene chloride (50 c.c.) at −80°. There was immediate formation of a white precipitate (11·40 g.) which was filtered off, washed with methylene chloride, and dried at 10 mm. (Found: B, 3·0; Cl, 58·6; Se, 33·1%). Evaporation of the filtrate gave selenium oxychloride (0·45 mol.) (Found: Cl, 42·2. Calc. for Cl_2OSe: Cl, 42·7%). Sublimation of the precipitate at 10 mm. gave selenium tetrachloride (9·9 g., 95%), m. p. 304° (Found: Cl, 64·0;

[1] Wise, *J. Amer. Chem. Soc.*, 1923, **45**, 1233.
[2] Smith, *Chem. Rev.*, 1938, **23**, 165.
[3] Sheldon and Tyree, *J. Amer. Chem. Soc.*, 1959, **81**, 2290.
[4] Agerman, Andersson, Lindqvist, and Zackrisson, *Acta Chem. Scand.*, 1958, **12**, 477.
[5] Gutmann and Himml, *Z. anorg. Chem.*, 1956, **287**, 199.
[6] Lenher, *J. Amer. Chem. Soc.*, 1922, **44**, 1664.

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Se, 35·3. Calc. for Cl_4Se: Cl, 64·2; Se, 35·8%), and a residue (0·9 g.) (Found: B, 30·5. Calc. for B_2O_3: 31·0%).

Aluminium trichloride (1 mol.) was suspended in a mixture of selenium oxychloride (2·50 g., 2 mol.) and methylene chloride (40 c.c.). The mixture was shaken at 20° for 6 hr. Filtration then gave a white powder (2·9 g.) which was washed with methylene chloride and dried at 10 mm. (Found: Cl, 55·1; Se, 30·8%). Evaporation of the filtrate gave selenium oxychloride (0·43 mol.) (Found: Cl, 42·3%). Sublimation of the precipitate at 10 mm. gave the tetrachloride (2·2 g., 88%), m. p. 304° (Found: Cl, 63·9; Se, 35·3%), and a residue of aluminium oxide (0·3 g.) (Found: Al, 52·5. Calc. for Al_2O_3: Al, 52·9%).

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THE NORTHERN POLYTECHNIC, HOLLOWAY ROAD,
LONDON, N.7.

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617. *An Aldobiouronic Acid Isolated from* Fagara xanthoxyloides *Gum.*

By F. G. TORTO.

EVIDENCE has been presented [1] for the occurrence of galactose, arabinose, and 4-*O*-methylglucuronic acid in the gum exuded by *Fagara xanthoxyloides* (Lam). Paper-chromatographic examination of the products of partial hydrolysis of the gum reveals the presence of an aldobiouronic acid, composed of galactose and 4-*O*-methylglucuronic acid residues, as well as a slow moving oligosaccharide (or oligosaccharides) composed of galactose and glucuronic acid residues.

Hydrolysis of the polysaccharide with 0·5N-sulphuric acid, followed by precipitation of the neutralised hydrolysate with methanol, gave a mixture of barium salts, from which the barium aldobiouronate was isolated by large-scale paper-chromatography as a white hygroscopic powder, $[\alpha]_D^{24}$ +86°.

The aldobiouronic acid was converted into a neutral disaccharide by reduction of the methyl ester methyl glycoside with potassium borohydride. Methylation of the disaccharide gave a derivative which on acid hydrolysis gave 2,3,6-tri-*O*-methylgalactose and 2,3,4,6-tetra-*O*-methylglucose. The aldobiouronic acid is therefore 4-*O*-(4-*O*-methyl-α-D-glucuronosyl)-D-galactose, the anomeric configuration following from the optical rotation. This aldobiouronic is a component of gum myrrh.[2] A 4-*O*-(4-*O*-methyl-D-glucuronosyl)-D-galactose occurs in gums of Khaya species.[3,4]

Experimental.—Paper chromatograms were run in (*a*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4) or (*b*) butanol–ethanol–water (5 : 1 : 4; upper phase). Sugars were detected with *p*-anisidine phosphate or aqueous ammonium molybdate. R_{gal} and R_G values are relative to the rates of migration of galactose and 2,3,4,6-tetra-*O*-methylglucose, respectively.

Isolation of aldobiouronic acid. Crude gum (60 g.) was heated in 0·5N-sulphuric acid (600 ml.) at 100° for 14 hr. The filtered solution was neutralised with barium carbonate, and then filtered, and the filtrate concentrated under reduced pressure to a light syrup (100 ml.), which was poured with stirring into methanol (1800 ml.). The precipitated barium salts were collected on a sintered-glass filter, washed thoroughly with methanol, and dried ($CaCl_2$) in a vacuum (yield 4·8 g.). On a paper chromatogram the product gave two spots, R_{gal} 0·69 and 0·23, as well as a trace of galactose. The same pattern of spots was obtained from a hydrolysate of a specimen of gum carefully purified by precipitation in acidified methanol.

[1] Torto, *Nature*, 1957, **180**, 864.
[2] Jones and Nunn, *J.*, 1955, 3001.
[3] Aspinall, Hirst, and Matheson, *J.*, 1956, 989.
[4] Aspinall, Johnston, and Stephen, *J.*, 1960, 4918.

A sample of the mixed barium salts was completely hydrolysed by 2N-sulphuric in a sealed tube at 100° for 24 hr. The neutralised solution, de-ionised with IR-120 H, gave galactose, glucuronic acid, glucurone, and 4-*O*-methylglucuronic acid on a chromatogram.

Large-scale paper-chromatography of the mixed barium salts (1 g.) gave barium aldobiouronate as a white hygroscopic powder (350 mg.), $[\alpha]_D^{24}$ +86° ± 1° (*c*, 0·5 in water) (Found: Ba, 15·8; OMe, 6·1. Calc. for $C_{26}H_{42}O_{24}Ba$: Ba, 15·7; 2OMe, 7·1%). Prolonged chromatography (90 hr.) with solvent (*a*) indicated that the material was homogeneous. Upon complete hydrolysis with 2N-sulphuric acid, it gave galactose and 4-*O*-methylglucuronic acid on the chromatogram. Only 4-*O*-methylglucuronic acid was detected in the hydrolysate of a specimen oxidised for several days with bromine water.

Isolation of 4-O-*methylglucuronic acid.* A portion of the mixed barium salts (0·9 g.) was treated with N-sulphuric acid (50 ml.), the mixture filtered, and the filtrate heated in a sealed tube at 100° for 18 hr. The filtered solution was neutralised with IR-4B resin, and the resin collected and washed till the washings were non-reducing. The uronic acids were recovered by stirring the resin with successive portions of dilute sulphuric acid till a slight excess of sulphuric acid was present. The combined solutions were treated with barium acetate till sulphate free. Barium sulphate was removed by filtration and the filtrate concentrated to a syrup, from which 4-*O*-methylglucuronic acid (20 mg.) was isolated by chromatography on large sheets of paper. The product was refluxed with 1% methanolic hydrogen chloride (10 ml.) and then neutralised with silver carbonate. The filtered solution was evaporated under reduced pressure to a syrup which was treated with concentrated ammonia (5 ml.) and kept at 0° for 24 hr. The solvent was evaporated, leaving a syrup which crystallised. The product was recrystallised several times from ethanol giving plates of the amide of methyl 4-*O*-methyl-α-D-glucuronoside, m. p. 232—233° (lit.,[2] 232°), $[\alpha]_D^{21}$ +145° (*c* 0·5 in water).

Identification of the aldobiouronic acid. Barium aldobiouronate (250 mg.) was refluxed with 1·8% methanolic hydrogen chloride (50 ml.) for 7 hr., neutralised with silver carbonate, and filtered. The filtrate was evaporated to dryness, the residue dissolved in water (5 ml.), and the solution added slowly to one of potassium borohydride (150 mg.) in water (2 ml.). After 2 hr., the excess of borohydride was destroyed by the addition of dilute acetic acid, the solution de-ionised with IR-120 H and IR-45 resins, and evaporated under reduced pressure to dryness. The syrup obtained was methylated three times with methyl sulphate and sodium hydroxide, and the product (after extraction of the acidified mixture with chloroform) was further methylated twice with methyl iodide and silver oxide, giving a yellow syrup (200 mg.), n_D^{26} 1·465 (Found: OMe, 54·9. Calc. for $C_{20}H_{38}O_{11}$: OMe, 54·6%). This material was hydrolysed with N-sulphuric acid (10 ml.) at 100° for 18 hr. The neutralised hydrolysate ($BaCO_3$), was extracted with chloroform, and the chloroform removed, giving a syrup (130 mg.) which was separated on Whatman 3MM paper into two fractions. The first fraction (35 mg.) had m. p. and mixed m. p. (with 2,3,4,6-tetra-*O*-methylglucose) 84°, $[\alpha]_D^{22}$ +83° (*c*, 0·5 in water). It was converted into the anilide, m. p. and mixed m. p. 137—138°. The second fraction (28 mg.), R_G (solvent *b*) 0·71, $[\alpha]_D^{21}$ +87° (*c*, 0·5 in water), was oxidised with bromine water (4 days). The product, isolated in the usual way, was recrystallised from ether–light petroleum, giving needles of 2,3,6-tri-*O*-methylgalactofuranolactone, m. p. 98—99° (lit.,[2] 98—99°), $[\alpha]_D^{22}$ −40°.

UNIVERSITY COLLEGE OF GHANA, LEGON, ACCRA. [*Received, February 27th*, 1961.]

618. *Some New Polydentate Arsenic Ligands.*

By T. E. W. HOWELL, S. A. J. PRATT, and L. M. VENANZI.

WHILE several bidentate phosphorus and arsenic ligands are known, only two tridentate ligands of these donor atoms, $CH_3{\cdot}As(CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}AsMe_2)_2$ and $Ph{\cdot}P(C_6H_4{\cdot}PEt_2\text{-}o)_2$ have been reported.[1,2] Furthermore, no tetradentate ligands of the heavy Group VB elements have been reported. We report here the preparation of two tridentate (Ia and b)

[1] Barclay and Nyholm, *Chem. and Ind.*, 1953, 378.
[2] Hart, *J.*, 1960, 3324.

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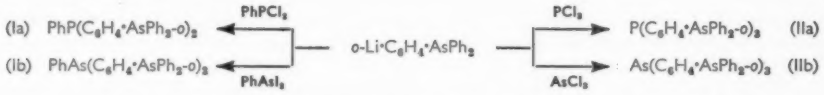
and two tetradentate ligands of phosphorus and arsenic (IIa and b), by the methods indicated in the scheme.



The compounds form white crystals, stable in air, and moderately soluble in aromatic hydrocarbons from which they can be recrystallised. Their complex-forming properties are being investigated.

Experimental.—o-*Diphenylarsinophenyl-lithium.* This was prepared by the method of Cochran *et al.*[3] The stoicheiometric amount of butyl-lithium was used to prevent the formation of undesirable by-products.

Bis-(o-*diphenylarsinophenyl*)*phenylphosphine* (Ia). Dichlorophenylphosphine (13 g.) in light petroleum (50 c.c.) was gradually added to the above lithium derivative (from 27 g. of *o*-bromophenyldiphenylarsine) in a nitrogen atmosphere. After hydrolysis the yellowish *product* was filtered off and recrystallised from anisole, yielding white crystals (8·5 g.), m. p. 238—240° (Found: C, 70·3; H, 4·4; As, 20·9; P, 4·7. $C_{42}H_{33}As_2P$ requires C, 70·6; H, 4·1; As, 21·0; P, 4·3%).

Bis-(o-*diphenylarsinophenyl*)*phenylarsine* (Ib). Di-iodophenylarsine (12·63 g.) in dry ether (30 c.c.) was added dropwise to the lithium derivative (from 23·96 g. of *o*-bromophenyldiphenylarsine). After hydrolysis and recrystallisation from tetrahydrofurfuryl alcohol the *product* formed white crystals, m. p. 235—236° (8 g.) (Found: C, 65·8; H, 4·6; As, 29·2. $C_{42}H_{33}As_3$ requires C, 66·2; H, 4·4; As, 29·5%).

Tris-(o-*diphenylarsinophenyl*)*phosphine* (IIa). This was prepared and purified as was its analogue (Ia). *o*-Bromophenyldiphenylarsine (25 g.) and phosphorus trichloride (2·2 c.c.) yielded a *product* (5·2 g.), m. p. 238—238·5° (Found: C, 67·8; H, 4·4; As, 24·0. $C_{54}H_{42}As_3P$ requires C, 68·5; H, 4·5; As, 23·7%).

Tris-(o-*diphenylarsinophenyl*)*arsine* (IIb) was prepared and purified analogously. *o*-Bromophenyldiphenylarsine (23·3 g.) and arsenic trichloride (1·69 c.c.) yielded the product (10 g.), m. p. 239—240° (Found: C, 65·7; H, 4·6; As, 30·2. $C_{54}H_{42}As_4$ requires C, 65·5; H, 4·3; As, 30·2%).

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Inorganic Chemistry Laboratory, University of Oxford. [*Received, March 1st,* 1961.]

[3] Cochran, Hart, and Mann, *J.*, 1957, 2816.

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